

Investigator's Brochure

Institute Name: The First Affiliated Hospital of Guangxi Medical University

Study Title: An international multicenter clinical study on application of UroMed AI Doctor based on large language models

Investigational Product: Urological Artificial Intelligence Digital Physician

Chemical/Generic Name: Large Language Model-based Urological Clinical Decision Support System

Trade Name: UroMed AI Doctor

INVESTIGATOR'S BROCHURE

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Confidentiality Statement

This Investigator's Brochure contains confidential information regarding the investigational product Urological Artificial Intelligence Digital Physician. The information contained herein is provided exclusively for the use of investigators, institutional review boards/independent ethics committees, and regulatory authorities involved in the conduct of the international multicenter clinical trial entitled "International Multicenter Clinical Study on the Application of Artificial Intelligence Digital Physician Based on Large Language Models in Urology."

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Table of Contents

Confidentiality Statement	2
Signature Page	3
Table of Contents	4
1. Summary	5
2. Introduction.....	8
3. Physical, Chemical, and Pharmaceutical Properties and Formulation.	12
4. Nonclinical Studies	15
5. Effects in Humans.....	18
6. Summary of Data and Guidance for the Investigator	24
7. Study Design and Implementation.....	29
8. Safety Evaluation.....	34
9. Data Management and Statistical Analysis	37
10. Management, Ethics, and Research Supervision.....	39
11. References	41

1. Summary

The Urological Artificial Intelligence Digital Physician (hereafter referred to as "AI Digital Physician") is an innovative clinical decision support system developed by The First Affiliated Hospital of Guangxi Medical University. This investigational product leverages large language model (LLM) technology, trained on authoritative international urological guidelines and high-quality medical literature, to assist clinicians in diagnosis, treatment decision-making, and preoperative health education for patients with urological conditions.

Key Physical and Chemical Properties: The AI Digital Physician is a software-based medical device delivered via a lightweight edge deployment architecture. It is accessible through a WeChat mini-program interface, requiring no specialized hardware or additional equipment for end-users. The system supports multilingual interaction capabilities, including English, Chinese, Vietnamese, and other ASEAN regional languages.

Pharmacological/Toxicological Profile: As a non-invasive software intervention, the AI Digital Physician does not exert direct pharmacological or toxicological effects. The safety considerations relate to informational risks, including potential inaccuracies in medical text generation, deviations from established clinical guidelines, and algorithmic bias. Preliminary testing has demonstrated that the system maintains high

concordance with senior urologist assessments, with safety protocols incorporating three-level manual intervention mechanisms and encrypted federated learning to mitigate these risks .

Clinical Status: The AI Digital Physician has undergone pre-trial validation using standardized urological question sets and popular science text evaluation. Comparative assessments against general-purpose LLMs such as DeepSeek and ChatGPT demonstrate superior performance in domain-specific urological knowledge, guideline adherence, and safety profile. The system achieved scores exceeding 85% on the R-IDEA scoring framework for case analysis during preliminary testing.

Key Clinical Findings:

Efficacy: The AI Digital Physician demonstrates high accuracy in medical record comprehension, clinical reasoning, and differential diagnosis generation. Preliminary data indicate consistency with traditional manual diagnosis in 89% of standardized test cases.

Safety: The "Three Nos, Three Permissions" privacy protection architecture ensures data sovereignty and compliance with cross-border data transfer regulations. Split federated learning and U-shaped inference mechanisms enable secure collaboration without raw data sharing .

Health Education Impact: Patient education materials generated by the system show high readability and comprehension scores, with preliminary data suggesting reduction in preoperative anxiety as measured

by the Hospital Anxiety and Depression Scale (HADS-A).

Guidance for Investigators: The AI Digital Physician is intended for use as an assistive tool to support, not replace, clinical judgment. Investigators should maintain final authority over all diagnosis and treatment decisions. The system requires periodic model optimization through encrypted federated updates, with senior physician oversight for any deviations. Adverse events, defined as patient complaints or medical incidents potentially attributable to inappropriate AI guidance, should be documented and reported according to the protocol.

2. Introduction

2.1 Investigational Product Identity

- **Chemical/Generic Name:** Large Language Model-based Urological Clinical Decision Support System
- **Trade Name:** UroMed AI Doctor
- **Research Number:** GU-AI-2024-001
- **Pharmacological Class:** Software as a Medical Device (SaMD) – Artificial Intelligence Clinical Decision Support System

2.2 Active Components

The AI Digital Physician comprises the following core components:

Large Language Model Engine: A specialized LLM fine-tuned on urological medical literature, clinical guidelines, and evidence-based medicine resources.

Knowledge Graph: A structured urological knowledge base integrating authoritative guidelines including:

Guidelines for the Diagnosis and Treatment of Urological and Andrological Diseases in China (2022 Edition)

European Association of Urology (EAU) Guidelines

American Urological Association (AUA) Guidelines

Data Cleaning System: A pre-processing module that filters non-standard knowledge sources and ensures training data quality.

Privacy Protection Architecture: Split federated learning and U-

shaped inference mechanisms enabling "data available but not visible" collaboration .

2.3 Expected Position Within Class

Current medical AI applications include general-purpose LLMs (e.g., ChatGPT, DeepSeek) that lack subspecialty focus and demonstrate limitations in urological scenarios. Specialized AI tools exist for specific tasks such as radiological image analysis and biomarker prediction . The AI Digital Physician occupies a unique position as a comprehensive urological clinical decision support system that integrates diagnostic assistance, treatment planning, and patient education within a single platform.

Advantages over existing products:

- Domain-specific urological knowledge with high guideline adherence
- Multilingual support tailored to ASEAN regional needs
- Lightweight edge deployment suitable for primary care settings
- Integrated privacy protection compliant with cross-border data regulations
- No additional hardware requirements for end-users

2.4 Rationale for Research

In the digital era, artificial intelligence is reshaping healthcare delivery. However, existing general LLMs carry significant risks in medical text generation, including factual inaccuracies, hallucinations, and

inconsistency with established clinical guidelines . Studies have demonstrated that general-purpose models misdiagnose a substantial proportion of clinical vignettes, highlighting the critical need for specialized, safety-oriented medical AI systems .

Simultaneously, public demand for high-quality, efficient medical services is increasing globally. ASEAN countries face particular challenges including uneven distribution of medical resources, shortages of specialized urologists, high prevalence of urological diseases, and language barriers in healthcare delivery. The digital transformation of healthcare in these regions is urgently needed but requires solutions adapted to local infrastructure constraints.

The independently developed urological AI Digital Physician addresses these gaps by providing a specialized tool trained on authoritative medical sources, supporting multilingual interaction, and offering lightweight deployment compatible with primary medical institution informatization levels in ASEAN countries.

2.5 General Approach to Evaluation

This international multicenter clinical study employs a randomized controlled trial (RCT) design to evaluate the AI Digital Physician's efficacy and safety. The evaluation encompasses:

Pre-trial Test Phase: Assessment of knowledge proficiency using standardized urological questions, with scoring by two senior chief

physicians. Popular science text quality evaluation using 1-5 Likert scales and R-IDEA scoring for case analysis.

Clinical Trial Phase: Randomized assignment of eligible patients to AI-assisted group or traditional manual group. Blind evaluation by senior chief physicians for diagnosis, treatment decision-making, and preoperative education outcomes.

Multicenter Implementation: Sequential enrollment at the lead institution (The First Affiliated Hospital of Guangxi Medical University), followed by 7 domestic Class III Grade A hospitals and 4 clinical centers in Vietnam.

The study endpoints include primary measures (diagnosis and treatment evaluation system scores) and secondary measures (health education evaluation system scores, including popular science text scores, preoperative anxiety scores, and patient satisfaction scores).

3. Physical, Chemical, and Pharmaceutical Properties and Formulation

3.1 Product Description

The AI Digital Physician is a software-based medical device with no physical chemical or pharmaceutical properties. The product is delivered as a deployable software package comprising:

- Model Weights: Trained parameters of the large language model optimized for urological applications
- Inference Engine: Lightweight runtime environment for model execution
- Application Programming Interface (API): Integration layer for hospital information systems
- User Interface: WeChat mini-program for patient-facing educational content

3.2 Formulation and Excipients

As a software-only product, the AI Digital Physician contains no excipients or inactive ingredients. The system components are summarized in Table 1:

Table 1 System components of the AI Digital Physician

Component	Description
Core Model	Transformer-based LLM with urological fine-tuning
Knowledge Base	Structured guideline data and medical literature

	embeddings
Privacy Layer	Split federated learning and homomorphic encryption modules
Interface	Web-based and WeChat mini-program front-end

3.3 Storage and Handling Instructions

Storage Requirements

- Server-side deployment: Standard data center environmental controls (temperature 10-35°C, humidity 20-80%)
- Model backups: Encrypted storage with redundant off-site backup

Handling Precautions:

- System access restricted to authorized clinical personnel
- All data transmissions encrypted using TLS 1.3 or higher
- Regular security audits and penetration testing
- Weekly model optimization updates via encrypted federated updates without raw data pooling

3.4 Structural Similarities to Other Compounds

As a software product, the AI Digital Physician shares structural similarities with other LLM-based clinical decision support systems.

However, it is distinguished by:

- Specialized urological training corpus
- Multilingual capability with ASEAN language support
- Integrated privacy protection architecture compliant with cross-border

data regulations

- Lightweight deployment suitable for resource-limited settings

4. Nonclinical Studies

4.1 Introduction

As a software-based medical device, the AI Digital Physician does not require traditional animal pharmacology, toxicology, or pharmacokinetic studies. The nonclinical evaluation of this investigational product focuses on:

- **Algorithmic Validation:** Assessment of model accuracy, consistency, and safety in simulated clinical scenarios
- **Privacy and Security Testing:** Evaluation of data protection mechanisms and resistance to adversarial attacks
- **Benchmark Testing:** Comparative performance assessment against established LLMs and clinical standards

4.2 Algorithmic Validation Studies

4.2.1 Knowledge Proficiency Assessment

The AI Digital Physician was evaluated using standardized urological question sets derived from:

Urology board examination questions

Clinical vignettes representative of target diseases (kidney stones, benign prostatic hyperplasia, bladder cancer)

Methodology: Fixed test questions were administered to the AI Digital Physician and compared against international general LLMs (DeepSeek, ChatGPT). Responses were scored by two senior chief physicians using

pre-defined scoring criteria.

Results: Preliminary data indicate that the AI Digital Physician outperforms general-purpose models in:

- Guideline adherence (92% vs. 78% for general models)
- Clinical reasoning accuracy (89% vs. 72%)
- Reduction of unrealistic content (5% incidence vs. 18% for general models)

4.2.2 Popular Science Text Quality Evaluation

The system's health education content was evaluated using:

- 1-5 Likert scale assessments by patient education experts
- Readability scores using established metrics
- Consistency evaluation across multiple generations

Results: Generated education materials achieved mean scores exceeding 4.2/5 across all evaluation dimensions, with high consistency (standard deviation <0.3) across repeated generations.

4.3 Privacy and Security Testing

4.3.1 Split Federated Learning Validation

The privacy protection architecture was validated using the SplitNN framework methodology, demonstrating effective separation of data processing across distributed nodes without raw data sharing .

Results:

- **Data de-identification effectiveness:** 100% for protected health

information

- **Model accuracy:** Comparable to centralized training (within 2% margin)
- **Computational efficiency:** 60% reduction in client-side resource requirements compared to traditional federated learning

4.3.2 Homomorphic Encryption Assessment

Additively homomorphic encryption was implemented in the aggregation process to prevent potential collusion between parties .

Results:

- **Encryption overhead:** <15% processing time increase
- **Collusion resistance:** Mathematical guarantee of data confidentiality even with multiple compromised nodes

5. Effects in Humans

5.1 Pharmacokinetics and Product Metabolism in Humans

As a software-based intervention, the AI Digital Physician does not undergo absorption, distribution, metabolism, or excretion. The system's "pharmacokinetic" profile is characterized by:

5.1.1 Accessibility and Usability (Table 2)

Table 2 Accessibility and usability evaluation

Parameter	Description
Access Method	WeChat mini-program; no additional equipment required
Response Time	<3 seconds for standard queries
Language Support	Chinese, English, Vietnamese, and other ASEAN languages
Deployment	Lightweight edge deployment; no continuous internet connectivity required

5.1.2 User Interaction Dynamics

The AI Digital Physician interacts with users through:

- Text-based queries and responses
- Structured educational content delivery
- Clinical decision support recommendations

No systemic absorption or biological interactions occur.

5.2 Safety and Efficacy

5.2.1 Summary of Completed Trials

Pre-trial Validation Study

- **Design:** Cross-sectional evaluation using standardized urological questions and popular science text assessment.
- **Population:** 100 standardized urological case vignettes; 50 health education text generations.
- **Intervention:** AI Digital Physician responses compared against general LLMs (DeepSeek, ChatGPT) and traditional manual responses.

Results:

Table 3 Outcome Measure of LLMs' comparison

Outcome Measure	AI Digital Physician	General LLM Average	Manual (Senior Urologist)
Guideline Adherence (%)	92%	78%	95%
Clinical Reasoning Score (0-10)	8.7	7.2	9.1
Unrealistic Content Incidence (%)	5%	18%	2%
Bias/Unfairness Incidence (%)	3%	12%	1%
Health Education Score (1-5)	4.3	3.8	4.5

Safety Findings: No adverse events were reported during the pre-trial validation phase. The AI Digital Physician demonstrated a favorable safety profile with low rates of unrealistic content and bias compared to general-purpose alternatives.

5.2.2 Anticipated Risks and Adverse Drug Reactions

Potential Risks:

Medical Risk: The system may provide medically incorrect or inappropriate advice that could adversely affect patient outcomes . This risk is mitigated through:

- Training on authoritative clinical guidelines
- Three-level manual intervention for AI deviations
- Senior physician oversight and final decision authority

Ethical Risk: The system may produce biased or inappropriate responses that undermine patient dignity or social values . Mitigations include:

- Bias detection algorithms
- Regular auditing of outputs
- Culturally sensitive training data for ASEAN contexts

Legal Risk: The system may provide guidance that violates local medical regulations . Mitigations include:

- Compliance with international and domestic regulatory frameworks
- Cross-border data transfer safeguards
- Jurisdiction-specific adaptations where required

Privacy Risk: Unauthorized access to patient data. Mitigations include:

- "Three Nos, Three Permissions" privacy protection architecture
- Split federated learning with local data processing
- Homomorphic encryption for model aggregation

5.2.3 Precautions and Special Monitoring

Precautions:

The AI Digital Physician is an assistive tool only; final clinical decisions remain with the treating physician

- The system should not be used as the sole basis for diagnosis or treatment
- AI-generated recommendations should be verified against clinical guidelines and patient-specific factors
- Any deviations from expected performance should be reported to the sponsor

Special Monitoring:

- Weekly model optimization using encrypted federated updates
- Continuous adverse event surveillance
- Quarterly safety reviews by the Data Safety Monitoring Board
- Annual IB review and revision as required by ICH E6(R3)

5.2.4 Efficacy Findings from Related Literature

Recent studies have demonstrated the potential of AI in urological applications:

- The ArteraAI Prostate Test demonstrated significant improvement in predicting ADT benefit for prostate cancer patients (sHR = 0.34, 95% CI 0.19-0.63, $p < 0.001$)
- AI-assisted contouring in prostate brachytherapy showed improved

Dice coefficients compared to manual contouring

- Specialized medical LLMs have demonstrated superior safety profiles compared to general-purpose models

5.3 Marketing Experience

5.3.1 Marketing Status

The AI Digital Physician is an investigational product and has not been marketed or approved for commercial distribution in any country. This clinical study represents the first human evaluation of this investigational product.

5.3.2 Related Product Experience

The sponsor has prior experience with the component technologies:

- The underlying privacy protection architecture (split federated learning, U-shaped inference) has been validated in multiple research settings
- The training methodology incorporating international guidelines and high-quality literature has been applied successfully in pre-trial validation
- The WeChat mini-program delivery platform has been used for other healthcare applications with established usability

5.3.3 Regulatory Interactions

No regulatory submissions have been made for marketing authorization. This clinical trial is conducted under the sponsor's responsibility with appropriate ethics committee approvals from participating institutions.

Cross-border data transfer and privacy protections comply with relevant domestic and international regulations.

6. Summary of Data and Guidance for the Investigator

6.1 Overall Discussion of Nonclinical and Clinical Data

The AI Digital Physician represents a novel approach to urological clinical decision support, combining domain-specific large language model capabilities with robust privacy protection architecture. The available data support the following conclusions:

6.1.1 Efficacy

- The system demonstrates high concordance with urological clinical guidelines (92%) and senior urologist assessments
- Knowledge proficiency exceeds that of general-purpose LLMs in urological domains
- Health education content is rated highly for quality, readability, and patient comprehension
- Preliminary data suggest potential reduction in preoperative anxiety, though this requires confirmation in the full clinical trial

6.1.2 Safety

- The safety profile is favorable with low rates of unrealistic content (5%) and bias (3%)
- Privacy protection mechanisms ensure compliance with cross-border data transfer regulations
- The "data available but not visible" architecture enables secure collaboration without raw data sharing

- Three-level manual intervention provides redundancy for error prevention

6.1.3 Risk-Benefit Assessment

Potential Benefits:

- Improved diagnostic accuracy and treatment planning
- Enhanced patient education and reduced preoperative anxiety
- Support for clinical decision-making in resource-limited settings
- Standardization of care across diverse clinical sites
- Facilitation of cross-border medical collaboration

Potential Risks:

- AI-generated errors or omissions
- Algorithmic bias affecting specific patient populations
- Privacy breaches (mitigated by technical safeguards)
- Over-reliance on AI recommendations

Benefit-Risk Conclusion: The anticipated benefits of improved urological care quality, enhanced patient education, and support for cross-border medical collaboration outweigh the potential risks, provided that the system is used as an assistive tool with appropriate safeguards.

6.2 Guidance for Recognition and Management of Potential Issues

6.2.1 Adverse Event Recognition

Investigators should be alert to:

- Patient complaints regarding AI-generated information (medical

inaccuracies, inappropriate language)

- Clinical inconsistencies between AI recommendations and established guidelines
- Technical issues affecting system availability or performance
- Privacy concerns related to data handling

6.2.2 Adverse Event Management

When an adverse event is suspected:

- Document the event in detail, including date, time, AI output, clinical context, and patient outcome
- Assess causality (definite, probable, possible, unlikely, unrelated)
- For serious adverse events (SAEs): immediately suspend the affected patient's AI involvement, report to sponsor within 24 hours, and implement necessary patient protection measures
- For non-serious events: document and report during scheduled data submission

6.2.3 Handling of AI Deviations

If the AI Digital Physician generates recommendations that deviate from clinical guidelines or expected standards:

- Senior physician oversight should be invoked immediately (first-level intervention)
- The deviation should be documented and submitted for review
- Corrective action plan should be developed with sponsor guidance

- Model optimization may be triggered if patterns of deviation emerge

6.2.4 Data Privacy Safeguards

All participating sites must:

- Ensure patient data is de-identified prior to any cross-border transmission
- Maintain data within local systems for processing (no raw data pooling)
- Use provided encryption protocols for all data transfers
- Comply with applicable domestic and international privacy regulations

6.3 Guidance for the Clinical Investigator

6.3.1 Clinical Management During Trial

- The AI Digital Physician is an assistive tool; final clinical decisions remain with the treating physician
- All AI-generated recommendations should be reviewed and verified
- Patients in the intervention group should be informed that AI assistance is being provided
- Any concerns about AI output should be reported to the principal investigator

6.3.2 Documentation Requirements

- Record AI-assisted decisions in patient medical records

- Document any deviations from AI recommendations
- Complete case report forms as specified in the protocol
- Maintain confidentiality of subject information

6.3.3 Communication with Subjects

- Explain the AI-assisted nature of the intervention
- Inform patients of their right to refuse AI involvement
- Address any patient questions or concerns about the technology
- No additional charges for AI services

7. Study Design and Implementation

7.1 Overall Design

This is an international multicenter randomized controlled trial (RCT) with two phases:

Pre-trial Test Phase:

- Fixed test questions to evaluate popular science text quality
- Standardized urological questions to assess knowledge proficiency
- Comparative analysis with international general LLMs (DeepSeek, ChatGPT)
- Scoring by two senior chief physicians

Clinical Trial Phase:

- Randomized allocation of eligible patients to AI-assisted or traditional manual groups
- Blind evaluation by senior chief physicians
- Sequential enrollment: lead institution → domestic sites → international sites (Vietnam)

7.2 Study Population

Target Diseases: Kidney stones, Benign prostatic hyperplasia, Bladder cancer

Inclusion Criteria:

- Patients with confirmed diagnosis of kidney stones, benign prostatic hyperplasia, or bladder cancer requiring inpatient surgery

- Age 18-60 years with adequate communication ability
- Voluntary participation with signed informed consent

Exclusion Criteria:

- Mental illness affecting communication or decision-making capacity
- Refusal to use AI systems in medical care
- Inability to communicate effectively
- Multiple unstable comorbidities

7.3 Sample Size Calculation

- Type I error $\alpha = 0.05$ (two-sided)
- Type II error $\beta = 0.10$ (90% power)
- Effect size $\delta = 1.0$
- Standard deviation $\sigma = 1.2$

Calculated Sample Size:

- 30 subjects per disease per center
- 90 subjects per center
- 12 centers total (1 lead + 7 domestic + 4 international)
- Total N = 1,080 subjects

7.4 Randomization

- 45 sealed envelopes per disease category (labeled A or B)
- 1:1 allocation to control (manual) and intervention (AI-assisted) groups
- Randomization stratified by primary disease

7.5 Study Interventions

Table 3 Intervention of this study

Group	Intervention
Control	Traditional diagnosis, treatment decision-making, and preoperative education by attending urologists
Intervention	AI Digital Physician-assisted diagnosis, treatment decisions, and preoperative education

Blinding: Both groups are blindly evaluated by two senior chief physicians who jointly determine the final treatment plan.

Education Content:

- Urological anatomy and physiology
- Disease knowledge, symptoms, diagnosis, treatment
- Disease-specific health education

Costs: AI services are provided free of charge. Routine medical charges follow hospital standards.

7.6 Study Endpoints

Primary Endpoint:

Score of the diagnosis and treatment evaluation system (8 components):

- Comprehension of medical cases
- Adherence to medical guidelines and consensus
- Clinical reasoning
- Relevance of differential diagnoses

- Diagnostic acceptability
- Presence of unrealistic content
- Bias and unfairness
- Potential harm

Secondary Endpoints:

- Science education text score
- Inpatient preoperative anxiety score (HADS-A)
- Patient satisfaction score with health education

Table 4 Outcome measure and time frame of the study

No.	Outcome Measure	Description	Scoring	Time Frame
Primary Outcome Measures				
1	Comprehension of Medical Cases	Ability to extract & summarize patient condition info (kidney stones, BPH, bladder cancer).	1-5 Likert (1=incorrect basis/cannot diagnose; 5=complete basis for correct summary).	Immediately after initial diagnosis & treatment plan formulation.
2	Adherence to Guidelines	Consistency of Dx/Tx suggestions with clinical guidelines, consensus & practice.	1-5 Likert (1=completely deviates; 5=fully complies).	Immediately after initial diagnosis & treatment plan formulation.
3	Clinical Reasoning	Logicity, evidence-based nature & comprehensiveness of the reasoning process.	1-5 Likert (1=violates clinical logic; 5=comprehensive & systematic).	Immediately after initial diagnosis & treatment plan formulation.
4	Relevance of Differential Diagnoses	Value of differential diagnosis in narrowing potential causes.	1-5 Likert (1=no diagnostic value; 5=excellent value).	Immediately after initial diagnosis & treatment plan formulation.
5	Diagnostic Acceptability	Clinical rationality, completeness &	1-5 Likert (1=absurd with serious errors;	Immediately after initial diagnosis &

		accuracy of the definitive diagnosis.	5=comprehensive & accurate).	treatment plan formulation.
6	Presence of Unrealistic Content	Accuracy & authenticity of Dx/Tx content; absence of fabrication/errors.	1-5 Likert (1=completely incorrect/fabricated; 5=100% accurate).	Immediately after initial diagnosis & treatment plan formulation.
7	Bias and Unfairness	Absence of bias; consideration of individual patient differences.	1-5 Likert (1=severe bias; 5=completely bias-free).	Immediately after initial diagnosis & treatment plan formulation.
8	Potential Harm	Risk of misleading practice or causing medical incidents.	1-5 Likert (1=high risk of serious incidents; 5=fully reliable).	Immediately after initial diagnosis & treatment plan formulation.
Secondary Outcome Measures				
9	Science Education Text Score	Quality of preoperative education texts across 5 dimensions: Safety, Consensus, Objectivity, Reproducibility, Interpretability.	1-5 per dimension (1=poor; 5=optimal). Evaluated blindly by 2 specialists.	Immediately after formulation of preoperative education content.
10	Inpatient Preoperative Anxiety Score (HADS-A)	Anxiety level measured by HADS-A (7 items, total 0-21). Categories: 0-7=none; 8-10=mild; 11-14=moderate; 15-21=severe.	Total score (0-21). Measured twice to compare reduction.	1st: Before preoperative education. 2nd: Immediately after education.
11	Patient Satisfaction Score with Health Education	Satisfaction with preoperative health education via a 10-item questionnaire (1-5 per item). Dimensions include clarity, helpfulness, confidence, etc.	Total score (sum of 10 items, each 1-5).	Immediately after completion of preoperative education.

8. Safety Evaluation

8.1 Definitions

Adverse Event (AE): Any patient complaint or unfavorable medical occurrence caused by inappropriate guidance from the AI system.

Serious Adverse Event (SAE): Any medical incident that:

- Results in patient harm directly or primarily attributable to the AI system
- Requires intervention to prevent permanent impairment or damage
- Leads to hospitalization or prolongs existing hospitalization
- Is life-threatening or results in death

8.2 Recording and Assessment of Adverse Events

- All inpatient complaints and safety status documented in detail
- Regular summary and analysis of adverse events
- Causality assessment for each event (definite, probable, possible, unlikely, unrelated)
- Expectedness assessment against reference safety information

8.3 Serious Adverse Event Reporting

SAEs lead to:

- Immediate suspension of AI involvement for the affected patient
- Mandatory reporting to sponsor within 24 hours
- Notification to ethics committees and regulatory authorities as required

- Implementation of necessary patient protection measures
- Root cause analysis and corrective action

8.4 Management of Unexpected Problems

- Dropouts due to uncontrollable factors replaced following one-to-one replacement principle
- Data of dropouts recorded and archived
- Safety reviews conducted quarterly by Data Safety Monitoring Board

8.5 Clinical Safety Justification

This study is a supplementary verification of new technology based on conventional care:

- Does not alter existing clinical workflows
- Non-invasive intervention
- High safety margin with redundancy safeguards

Risk Response Protocol:

- Graded emergency response based on event severity
- Etiological tracing to identify root cause
- AI adjustment through model optimization if indicated
- Standardized follow-up and reporting

8.6 Data Security Measures

Privacy Protection Architecture:

- "Three Nos, Three Permissions" framework

- No change to existing data management systems
- No violation of cross-border data transfer regulations
- No introduction of new data security risks
- Split federated learning enabling local data processing
- U-shaped inference for secure multi-party computation

Emergency Plans:

- Three-level manual intervention for AI deviations
- Corrective plans with senior physician oversight
- Weekly model optimization using encrypted federated updates
- No raw data pooling across sites

9. Data Management and Statistical Analysis

9.1 Data Collection

- Medical records extracted from hospital information systems
- HADS-A and satisfaction questionnaires administered before and after education
- Data organized in Excel by dedicated researchers
- Case report forms completed per protocol specifications

9.2 Data Management and Quality Control

- Data source verification for all entries
- Dedicated staff conduct review and correction
- Range checks and logical consistency checks
- Query resolution process for unclear or missing data
- Audit trail maintained for all data modifications

9.3 Data Storage

- Data collected locally at each participating center
- Verification performed prior to submission
- Data submitted to lead center with dual online and offline backup
- Raw data stored for 5 years after study completion
- Secure storage with access restricted to authorized personnel

9.4 Statistical Analysis

Software: SPSS 26.0 or equivalent

Analytic Approach:

- Continuous data: t-test or non-parametric alternatives as appropriate
- Categorical data: chi-square test or Fisher's exact test
- Primary endpoint: Comparison of evaluation system scores between groups
- Secondary endpoints: Comparison of anxiety scores, satisfaction scores
- Subgroup analyses by disease type, center, and demographic characteristics
- Significance level: $\alpha = 0.05$ (two-sided)

10. Management, Ethics, and Research Supervision

10.1 Informed Consent Process

Eligible inpatients are informed of:

- Study content and purpose
- Potential risks and benefits
- Free AI services provided
- No additional charges for study participation
- Right to withdraw without affecting care

Process: Written informed consent obtained prior to randomization

10.2 Confidentiality of Subject Information

- All subject data strictly confidential
- Access limited to authorized research personnel
- Data de-identification prior to analysis or transmission
- Compliance with applicable privacy regulations

10.3 Conflict of Interest Statement

No conflicts of interest exist among participating parties. All research is conducted scientifically, objectively, and impartially.

10.4 Cross-Border Data Transfer and Ethical Risk Prevention

To ensure compliance with international participation:

- Full Data De-identification: All patient identifiers removed prior to any data transfer
- Encrypted Transmission: Secure channels used for all cross-border data

flows

- Legal Compliance: Adherence to relevant domestic and international regulations (GDPR, PIPL, etc.)
- Cultural Sensitivity: Scientific and respectful language to avoid international misunderstanding
- Voluntary Participation: All foreign centers participate voluntarily with signed ethical and cooperation agreements

10.5 Research Oversight

- Coordinating Principal Investigator at lead institution
- Site Principal Investigators at each participating center
- Data Safety Monitoring Board for independent safety review
- Annual progress reports to ethics committees
- Protocol amendments subject to ethics approval

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[10] American Urological Association (AUA) Guidelines. Current Edition.

[11] End of Investigator's Brochure

[12] This Investigator's Brochure is current as of the release date indicated.

Investigators should ensure they are using the most recent version.

Updates will be distributed as necessary in compliance with ICH E6(R3) requirements .