Protocol & ICF (GXMU-PCa-AI-KY20260016)

Document 1: Study Protocol

Document Version: V1.0

Effective Date: January 28, 2026

Unique Protocol ID: GXMU-PCa-AI-KY20260016

Official Study Title: A Multicenter Study of a Deep Learning Model Based on Spatial Registration of Multimodal Imaging and Digital Pathology for Predicting Clinically Significant Prostate Cancer

Brief Title: Multimodal Imaging and Digital Pathology for Prostate Cancer Prediction

Study Type: Observational, prospective and retrospective multicenter cohort study

Sponsor: Guangxi Medical University

Principal Investigator: Fubo Wang, Professor, Doctoral Tutor of Medical Science, Guangxi Medical University

Ethics Approval Number: KY20260016

Ethics Committee: Medical Ethics Committee of Guangxi Medical University

Study Start Date: May 30, 2025

Primary Completion Date: June 30, 2030

Full Study Completion Date: December 31, 2030

Estimated Enrollment: 3000 participants

Study Status: Recruiting

Target Follow-up Duration: 12 years

1. STUDY BACKGROUND AND RATIONALE

Prostate cancer is one of the most common malignant tumors in elderly males globally. Clinically significant prostate cancer (csPCa) is closely correlated with tumor progression, distant metastasis and cancer-related mortality. Accurate preoperative identification and risk stratification of csPCa remain major clinical challenges.

Multiparametric magnetic resonance imaging (mpMRI) and transrectal ultrasound (TRUS) are standard preoperative imaging modalities for patients with suspected prostate cancer. The PI-RADS v2.1 scoring system is widely adopted for lesion risk evaluation in clinical practice. Nevertheless, conventional imaging assessment fails

to fully reflect microscopic pathological heterogeneity, thereby resulting in frequent unnecessary prostate biopsies, inconsistent diagnostic accuracy, and potential overdiagnosis or underdiagnosis.

Digital whole-slide images (WSI) of pathological specimens provide high-resolution microscopic pathological features and serve as the diagnostic gold standard for prostate cancer. Spatial inconsistency between macroscopic imaging lesions and microscopic pathological changes restricts precise correlation of imaging manifestations with pathological grading results.

Artificial intelligence and deep learning techniques support high-throughput feature extraction and multimodal data fusion. Spatial registration algorithms enable accurate alignment between preoperative imaging lesions and postoperative microscopic pathological structures, which facilitates the construction of precise and interpretable diagnostic models for prostate cancer.

This multicenter observational study is designed to establish and validate a multimodal deep learning prediction model based on spatial registration of mpMRI, TRUS and digital pathological WSI. The model is intended to achieve non-invasive and accurate prediction of csPCa, standardize non-invasive risk stratification, reduce unnecessary prostate biopsy procedures, and provide evidence for optimizing clinical diagnostic and therapeutic decision-making.

2. STUDY OBJECTIVES

Primary Objective: To construct and validate a transformer-based multimodal deep learning model for the prediction of clinically significant prostate cancer using spatially registered multimodal imaging and digital pathology data. The area under the receiver operating characteristic curve (AUC) is applied to evaluate the diagnostic discriminative ability of the model.

Secondary Objectives: (1) To analyze the spatial correlation between macroscopic imaging characteristics and microscopic pathological heterogeneity of prostate lesions; (2) To validate the generalization performance of the model through internal cross-validation, external multicenter independent validation and international public dataset validation; (3) To evaluate the clinical application value and net clinical benefit of the model via decision curve analysis and clinical impact curve analysis; (4) To verify the clinical value of the model in optimizing prostate biopsy strategies, reducing unnecessary puncture and overtreatment, and improving early precise diagnosis and risk stratification of prostate cancer.

3. STUDY DESIGN

This is a prospective and retrospective multicenter observational cohort study. No additional clinical interventions, experimental drugs or medical devices are applied to enrolled participants. Only routine standard-of-care clinical data, imaging data and pathological data are collected and analyzed.

The study population consists of two cohorts: a retrospective historical cohort and a

prospective newly enrolled cohort. All eligible participants receive standardized preoperative mpMRI and TRUS examinations, followed by clinically indicated prostate biopsy or radical prostatectomy with definitive pathological diagnosis.

All collected high-quality multicenter data are applied for model construction, spatial registration, multimodal feature fusion, model training, internal cross-validation and external multicenter independent validation.

4. STUDY POPULATION AND ELIGIBILITY CRITERIA

Study Population: Consecutive male subjects aged 40 to 90 years with suspected prostate cancer who complete standard preoperative mpMRI and TRUS examinations and receive subsequent prostate biopsy or radical prostatectomy with complete pathological diagnosis. The population includes retrospective historical cases and prospective newly enrolled cases with complete clinical, imaging and pathological data.

Inclusion Criteria: (1) Male subjects aged 40 to 90 years; (2) Subjects scheduled for or having undergone prostate biopsy or radical prostatectomy; (3) Subjects completing standard preoperative mpMRI and TRUS examinations; (4) Subjects with complete postoperative pathological results including Gleason score and ISUP grading; (5) Prospective participants providing valid written informed consent.

Exclusion Criteria: (1) Subjects with a history of pelvic radiation therapy or prior radical prostatectomy; (2) Subjects with incomplete or low-quality mpMRI or TRUS images with motion artifacts, missing sequences or unrecognizable lesions; (3) Subjects with concurrent other primary malignant tumors; (4) Subjects with severe systemic diseases interfering with prostate lesion evaluation; (5) Subjects with incomplete clinical, imaging or pathological data; (6) Subjects with MRI contraindications including incompatible metallic implants and severe claustrophobia.

5. DATA COLLECTION

Collected clinical data include age, BMI, PSA-related serological indicators and PI-RADS v2.1 scoring results. Imaging data cover preoperative mpMRI and TRUS images. Pathological data include digital whole-slide images of prostate biopsy or radical prostatectomy specimens, corresponding Gleason score and ISUP grading results. All data are fully de-identified to guarantee participant privacy and data security.

6. MODEL CONSTRUCTION AND VALIDATION

Biomechanically constrained non-rigid spatial registration technology is adopted to achieve precise spatial alignment between preoperative multimodal imaging lesions and postoperative digital pathological WSI. A transformer-based multimodal deep learning fusion model is constructed to explore potential correlations between macroscopic imaging manifestations and microscopic pathological heterogeneity, so as to establish an interpretable artificial intelligence prediction framework for csPCa.

Comprehensive model validation is performed through internal cross-validation, external multicenter independent validation and international public dataset verification. AUC is used as the primary indicator to evaluate model diagnostic performance. Decision curve analysis and clinical impact curve analysis are conducted to assess clinical practicability and net benefit of the model for clinical decision-making.

7. OUTCOME MEASURES

Primary Outcome Measure: AUC of the multimodal deep learning model for predicting clinically significant prostate cancer at the time of baseline imaging and pathological data collection.

8. DATA MANAGEMENT AND PRIVACY PROTECTION

All participant data are de-identified without reserved personal identifiable information. Data storage, processing and analysis strictly comply with institutional ethical specifications and relevant national regulations. Individual participant data are not shared publicly due to ethical and institutional restrictions.

9. SAFETY MONITORING

This study is observational and does not bring additional physical risks or intervention-related harm to participants. A Data Monitoring Committee is established to supervise study quality, data integrity and scientific validity throughout the entire research period.

10. STUDY DURATION

Study Start Date: May 30, 2025 (Actual)

Primary Completion Date: June 30, 2030 (Anticipated)

Full Study Completion Date: December 31, 2030 (Anticipated)

11. ETHICS STATEMENT

This study has been reviewed and approved by the Medical Ethics Committee of Guangxi Medical University (Approval No. KY20260016). All prospective participants provide written informed consent before enrollment. All study procedures strictly adhere to the Declaration of Helsinki and standard clinical research ethical principles.

Document Version: V1.0

Release Date: January 28, 2026

Document 2: Informed Consent Form

Document Version: V1.0

Effective Date: January 28, 2026

Study ID: GXMU-PCa-AI-KY20260016

Study Title: A Multicenter Study of a Deep Learning Model Based on Spatial Registration of Multimodal Imaging and Digital Pathology for Predicting Clinically Significant Prostate Cancer

Sponsor Institution: Guangxi Medical University

Ethics Approval Number: KY20260016

1. INTRODUCTION

This informed consent form provides detailed information for participation in a multicenter observational clinical study. The study focuses on the construction and validation of an artificial intelligence prediction model for clinically significant prostate cancer based on multimodal imaging and digital pathology spatial registration. Study participation is completely voluntary.

2. STUDY BACKGROUND AND PURPOSE

Prostate cancer is a common malignant tumor in elderly males. Clinically significant prostate cancer is the key factor leading to tumor progression and adverse prognosis. Conventional imaging evaluation has limitations in precise risk stratification, which may cause unnecessary prostate biopsy and inaccurate diagnosis.

This study aims to construct a high-precision artificial intelligence prediction model by integrating preoperative mpMRI, TRUS and postoperative digital pathological whole-slide images. The model is expected to realize non-invasive accurate prediction of clinically significant prostate cancer, optimize clinical biopsy decision-making, and provide evidence for individualized prostate cancer diagnosis.

3. STUDY PROCEDURES

This is an observational study without any experimental intervention. No additional drugs, operations or medical devices will be applied to participants beyond routine clinical diagnosis and treatment. Eligible participants will receive standard preoperative mpMRI and TRUS examinations, followed by clinically indicated prostate biopsy or radical prostatectomy. Routine clinical data, imaging images and pathological results will be collected for model construction and validation.

4. DATA COLLECTION CONTENT

Collected data include routine clinical baseline information, PSA-related indicators, PI-RADS v2.1 scores, preoperative mpMRI and TRUS images, and postoperative

pathological results including Gleason score and ISUP grading. All data will be fully de-identified to protect personal privacy.

5. POTENTIAL BENEFITS

No direct personal benefits are provided for individual participants. The findings of this study can improve the accuracy of preoperative prediction for clinically significant prostate cancer, reduce unnecessary clinical biopsy procedures, optimize clinical diagnostic workflows, and benefit future patients with suspected prostate cancer.

6. POTENTIAL RISKS

No additional research-related risks or physical discomfort will occur. All examinations and procedures involved in this study are routine standard clinical operations. Data collection will not affect participants' routine diagnosis, treatment and prognosis, and will not increase any physical or psychological burden.

7. PRIVACY AND CONFIDENTIALITY

All participant data will be strictly de-identified and stored in encrypted form. All research staff have signed confidentiality agreements. Personal private information will not be leaked, published or used for non-research purposes. All published research results will be presented with aggregated statistical data without individual participant information. Individual participant data will not be shared publicly due to ethical and institutional restrictions.

8. PARTICIPATION RIGHTS

Participation in this study is voluntary. Participants have the right to refuse enrollment or withdraw from the study at any time without any penalty or negative impact on subsequent clinical diagnosis and treatment. Participants have the right to consult relevant study information at any time during the research period.

9. CONTACT INFORMATION

Principal Investigator: Fubo Wang, Professor, Doctoral Tutor of Medical Science, Guangxi Medical University

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Ethics Committee Contact: Medical Ethics Committee of Guangxi Medical University

Ethics Phone: +86 13222728173

Ethics Email: gxmulunli@163.com

10. ETHICS APPROVAL

This study has been approved by the Medical Ethics Committee of Guangxi Medical University (Approval No. KY20260016). All study procedures comply with the Declaration of Helsinki and international clinical research ethical guidelines.

11. CONSENT STATEMENT

The undersigned participant has fully understood the study purpose, procedures, potential benefits and relevant risks of this research. All questions have been answered clearly. The participant voluntarily agrees to participate in this study and authorizes the research team to collect and analyze routine clinical, imaging and pathological data for this research project.

Participant Signature: _____

Date: _____

Researcher Signature: _____

Date: _____

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Medical Ethics Committee Review Approval Document, Guangxi Medical University

Approval No.: KY20260016

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<tr><td>Study Category</td><td colspan="5">☑ Scientific Research Project Application</td></tr>
<tr><td>Applicant Institution</td><td colspan="5">Center for Genomic and Personalized Medicine, Guangxi Medical University</td></tr>
<tr><td>Principal Investigator</td><td>Wang Fubo</td><td>Title</td><td>Professor</td><td>Specialty</td><td>Urology</td></tr>
<tr><td>Co-Investigators</td><td>Wang Fubo, Chen Wei, Zhang Bulin, Xu Aiming, Wang Fei, Zhang Duobing, Chen Junyi, Yang Bin, Huang Gang, Xu Bin, Yu Xiaoxiang, Zhuo Tao, Sun Jie, et al.</td><td>Participating Institutions</td><td>The First Affiliated Hospital of Guangxi Medical University; The First Affiliated Hospital of Wenzhou Medical University; Liuzhou People’s Hospital; Jiangsu Provincial People’s Hospital; Hainan General Hospital, etc.</td><td colspan="2">Is Guangxi Medical University the Lead Site/Sponsor Institution?
☑ Yes
☐ No</td></tr>
<tr><td>Reviewed Documents</td><td colspan="5">☑ 1.Project Application/Research Protocol ☑ 2.Ethics Application Form
☑ 3.Informed Consent Form ☑ 4.Curriculum Vitae of Principal Investigators
☐ 5.Project Approval Notice ☐ 6.Project Collaboration Agreement ☐ 7.Other</td></tr>
<tr><td>Review Type</td><td colspan="5">☑ Expedited Review ☐Full Board Review</td></tr>
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☐ Re-Review Required with Modifications ☐ Disapproved
☐ Suspension or Termination of Approved Trial/Study</td></tr>
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Seal	Guangxi Medical University Medical Ethics Committee (Seal) January 28, 2026
Additional Notes	This review approval is only for the purpose of scientific research project application. It certifies that the project complies with the requirements of the Measures for the Ethical Review of Biomedical Research Involving Human Subjects and relevant national laws and regulations of the People's Republic of China.