

**Precision Radiotherapy with novel Technologies and
Strategies for Refractory Brain Metastases: A Multicenter
Prospective Study**

Study Institution: Cancer Hospital, Chinese Academy of Medical Sciences

Principal Investigator: Nan Bi

Email: binan_email@163.com

Date: 2026/4/1

NCT number:

Study Objectives

Conventional image-guided techniques (such as cone-beam CT) have poor soft tissue contrast and unsatisfactory treatment outcomes. MRgART offers high-resolution imaging of brain tissue and, by acquiring daily MR images, achieves real-time monitoring of tumor position and volume changes during treatment, potentially improving local control rates for brain metastases, reducing toxicities, and translating into survival benefits. Our research team has already conducted a phase II prospective study with favorable results: 1-year local control rate for intracranial brain metastases of 100%, significantly superior to historical controls of conventional radiotherapy, no severe late toxicities, and real-time individualized precision treatment. Based on these phase II results, this phase III single-arm prospective study was designed.

This study aims to conduct a multicenter prospective study to establish an MR-guided adaptive radiotherapy (MRgART) technical platform, enabling real-time monitoring of tumor position and volume changes and individualized plan adaptation. Through technological innovation, we aim to significantly improve local control rates for large and complex brain metastases while reducing severe adverse effects such as radiation brain necrosis, laying the technical foundation for precise and safe treatment.

This study will establish a new adaptive radiotherapy (ART) system for brain metastases based on per-fraction MR images, using ART to improve target dose

coverage and reduce radiation doses to organs at risk such as normal brain tissue. It is anticipated to validate the phase II findings of high local control, low toxicity, and significantly prolonged survival. Based on the results, combined with multicenter clinical practice and application experience, domestic and international expert symposiums will be conducted, and a multicenter consensus on MRI-linac guided adaptive radiotherapy for brain metastases from lung cancer will be developed.

Additionally, recognizing that MRI generates high noise levels and that repeated treatments without adequate hearing protection may cause hearing damage, this study will collect hearing-related scales from patients before, during, and after treatment (pure-tone audiometry in otolaryngology or self-test via mini-program) to explore the impact of strict vs. non-strict hearing protection on changes in hearing scales, treatment interruption, and repeated setup.

Compared to conventional cone-beam CT-guided radiotherapy, MRI-guided adaptive radiotherapy still has shortcomings: MR image acquisition is slow; manual registration with CT images, manual re-contouring, manual plan calculation, and triple review by physicians, physicists, and therapists are required. Currently, each patient requires approximately 40–60 minutes from lying on the couch to treatment completion; setup errors or large target changes requiring adaptive re-contouring may take even more time, posing challenges to patients' physical and mental state, and limiting applicability in patients with altered consciousness, elderly/frail

patients, or those unable to cooperate. It also consumes substantial medical resources.

To address this, our group plans to develop an AI-assisted target contouring, treatment planning, and decision-making system, establishing a full-process AI-assisted model for MRgART in lung cancer brain metastases, and compare its efficacy and treatment time differences with manual radiotherapy delivery.

Additionally, we will explore the feasibility of exempting a small subset of patients (approximately 10–20 cases) from conventional CT and MR simulation, contouring targets on simulation CT/MRI images, and directly using ATS (adaptive target shaping based on interfractional deformation) for treatment planning within the MRgART workflow.

Study Design

This study aims to establish a new MRgART system to address the technical bottlenecks of low local control rates and high risk of radiation brain necrosis for large or complex brain metastases. The study will collaborate with multiple domestic centers, prospectively collect clinical and imaging data, and conduct a phase III non-randomized, multicenter, open-label, single-arm, exploratory clinical trial.

Research Tasks and Endpoints

1. Establish MRgART treatment workflow, standardized target contouring and plan adaptation protocols, real-time monitoring of tumor position/volume changes, and individualized plan adjustments.
2. Compare MRgART with conventional stereotactic radiotherapy (historical control) in local control rate, severe radiation brain necrosis incidence, and quality of life, exploring a new precise and safe radiotherapy model.
3. Establish a multicenter data sharing and quality control platform, forming generalizable clinical operation standards and expert consensus.
4. Establish a hearing assessment database during radiotherapy, highlighting the importance of hearing protection during MRI-guided radiotherapy, and explore optimal hearing protection methods.
5. Establish an AI-assisted full-process adaptive radiotherapy system for MRgART.
6. Enroll 10–20 patients to evaluate the feasibility of 免除 CT/MRI simulation and using diagnostic images directly for target design and planning, 免除 traditional three-point mask immobilization, and compare safety, efficacy, dose distribution, and treatment time with conventional methods (remaining 180–190 patients).

Key Problem to Solve

How to maximize local control for large brain metastases while minimizing severe adverse effects such as radiation brain necrosis, improve treatment efficiency,

reduce resource waste, and promote the implementation of new precise and safe technologies.

Hypothesis

MRgART significantly improves local control for large/complex brain metastases while reducing severe adverse effects such as radiation brain necrosis. Hearing can be well protected during MRgART. The AI-driven automatic treatment decision system significantly accelerates MRgART delivery, with safety and efficacy approaching or exceeding manual levels. Treatment without CT/MRI simulation is safe, tolerable, with no significant difference in efficacy and greatly shortened preparation time.

Treatment Regimen

Patients receive 1.5T MR-Linac guided adaptive radiotherapy (52 Gy/13 fractions or individualized fractionation adjustments based on tumor size/location). Before each treatment, real-time MRI monitoring of tumor volume/position changes, online adjustment of GTV/PTV and dose distribution, achieving precise individualized irradiation.

Target and plan changes during treatment will be collected to develop an AI automatic treatment decision system (DLAS or machine learning models) with manual verification, training:validation = 3:1, tested in 50 patients, comparing differences and safety before/after implementation.

10–20 patients will undergo rapid ATS-MRgART without CT/MRI simulation to evaluate tolerability, efficacy, and treatment time.

Primary Endpoint

2-year local control rate (LCR); median and 1-year LCR will also be reported.

Secondary Endpoints

- Intracranial progression-free survival (iPFS); median, 1- and 2-year iPFS
- Incidence of radiation brain necrosis (RN)
- Overall survival (OS); median, 1- and 2-year OS
- Disease control rate (DCR), objective response rate (ORR)
- Neurocognitive function changes (HVLT-R, MoCA)
- Quality of life (EORTC QLQ-C30)
- Adverse events (CTCAE v5.0 grading)
- Hearing impairment (HHIE scale and pure-tone audiometry classification)

Follow-up Schedule

Follow-up at 3, 6, 9, 12 months after treatment completion, then every 6 months until 2 years or death. Each follow-up includes brain MRI, physical examination, blood routine, biochemistry, tumor markers, and neurocognitive assessment.

Data Collection

Case report forms (CRF) for all patients including baseline data, treatment information, imaging assessments, and follow-up data.

Data Management

All centers enter data into a unified electronic database; the lead center is responsible for quality control and data verification. Regular data audits ensure completeness and accuracy. Data are encrypted and accessible only to researchers, complying with ethical and privacy requirements. A multicenter data sharing and quality control platform will be established.

Standardization and Consensus Formation

Our center will provide standardized patient, target, and plan data for comparison among participating centers. After feedback and discussion of differences, an SOP for target contouring and treatment planning will be formed. Based on the SOP, previous research, and this study's data, domestic and international expert meetings and symposiums will be held to form expert consensus or treatment standards, integrating the latest domestic and international research and guidelines.

AI Systems for Target Contouring, Treatment Decision, Plan Design, and Prognosis Assessment

Based on our previous phase II study, we have developed a deep learning-based automatic segmentation (DLAS) model for target and OAR contouring. Our physics department has published an auto-planning model based on secondary contoured targets. We will further explore AI models for ATP (adaptive target positioning) and ATS (adaptive target shaping) based on target changes, as well as prognostic AI models combining daily multimodal images and pre-treatment baseline data.