

Longitudinal MRI Response Phenotypes and Lesion-Level Local Control after Gamma Knife Radiosurgery for Breast Cancer Brain Metastases

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Case Report

Keywords: breast cancer brain metastases, Gamma Knife radiosurgery, longitudinal MRI, volumetric response phenotype, local control, treatment response assessment

Posted Date: October 7th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11035796/v1>

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Additional Declarations: No competing interests reported.

Abstract

Purpose

Serial magnetic resonance imaging (MRI) demonstrates heterogeneous lesion evolution after stereotactic radiosurgery. We characterized longitudinal volumetric response phenotypes after Gamma Knife radiosurgery (GKRS) for breast cancer brain metastases and examined their association with 12-month lesion-level local control.

Methods

This single-center retrospective study included 80 patients, 182 GKRS-treated lesions, and 819 serial MRI records. Local control was assessed within a prespecified 10–14-month window. Lesions were classified as complete response/disappearance, partial regression, stable control, or progression. Baseline correlates of local failure were evaluated using Bayesian mixed-effects logistic regression, with patient-clustered generalized estimating equations used for sensitivity analysis.

Results

Local control was evaluable in 103 lesions and longitudinal phenotype in 154. The four phenotypes comprised 24 complete responses/disappearances, 59 partial regressions, 44 stable controls, and 27 progressions. In the prespecified Bayesian model, larger baseline whole-tumor volume and peritumoral edema were associated with higher odds of local failure, whereas higher BED₁₀ was inversely associated; clustered sensitivity estimates retained the same directions but were less precise. Progression phenotype was strongly associated with local failure after accounting for within-patient clustering (odds ratio 27.08, 95% confidence interval 7.11–103.20; $p < 0.001$) and remained associated when classification was restricted to the 10–14-month window.

Conclusion

Longitudinal volumetric MRI phenotypes capture heterogeneous post-GKRS lesion evolution and identify a progression pattern closely associated with local failure. This framework may complement standard local-control assessment during post-treatment surveillance.

1. Introduction

Brain metastases are a major cause of neurologic morbidity in advanced breast cancer. Intracranial risk varies by molecular subtype and is particularly high in human epidermal growth factor receptor 2 (HER2)-positive and triple-negative disease [1, 2]. Prognosis is also shaped by performance status, intracranial disease burden, receptor discordance, and subtype switching [3–5]. Modern systemic agents, including

tucatinib-based therapy and trastuzumab deruxtecan, have demonstrated clinically meaningful intracranial activity in HER2-positive disease [6, 7]; nevertheless, local therapy remains central for patients with limited or clinically actionable brain metastases. Stereotactic radiosurgery (SRS), including Gamma Knife radiosurgery (GKRS), is guideline-supported and can avoid the neurocognitive burden of whole-brain radiotherapy in appropriately selected patients [8–12].

Local failure remains clinically relevant after SRS. Breast-cancer-specific series and subtype-specific cohorts have associated recurrence with lesion size, treatment factors, and tumor subtype [13–16]. However, analyses centered on patient-level survival or a single binary local-control endpoint may obscure lesion-to-lesion heterogeneity, because metastases in the same patient may disappear, regress, remain stable, or enlarge after treatment. Dose prescription is also influenced by lesion volume, location, previous treatment, and normal-tissue constraints. Lesion-level analyses should therefore evaluate imaging and treatment factors while accounting for within-patient clustering. Established dose-selection and comparative studies have linked prescription dose, target volume, and fractionation with local control and radiation necrosis [17–19]. A lesion-level analysis that accounts for clustering within patients is therefore needed to evaluate baseline imaging phenotype and treatment intensity together.

Serial MRI provides a complementary view of treatment response. The Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) criteria provide a standardized framework, but one-dimensional assessment can be difficult for small or irregular post-SRS lesions, and transient enlargement may represent tumor, radiation injury, or mixed treatment effect [20–23]. Volumetric longitudinal patterns may better describe how individual lesions evolve, but these patterns should be compared with a locked clinical endpoint rather than treated as interchangeable surrogate outcomes.

We therefore evaluated longitudinal volumetric MRI response phenotypes after GKRS for BCBM, assessed their relationship with 12-month lesion-level local control, and examined how baseline imaging features and biological dose contributed to local-failure risk.

2. Materials and Methods

2.1. Study Design and Cohort

This retrospective cohort study included consecutive patients with pathologically confirmed breast cancer and radiologically confirmed brain metastases who underwent Gamma Knife radiosurgery (GKRS) at West China Hospital, Sichuan University, between April 2021 and August 2025. Clinical and imaging follow-up data were reviewed through August 2026. Eligible patients had no more than 10 visible intracranial metastases before the index GKRS course, in accordance with institutional treatment practice and prospective evidence supporting SRS alone for carefully selected patients with up to 10 brain metastases [24], and had pretreatment contrast-enhanced T1-weighted MRI adequate for identification and volumetric delineation of at least one treated lesion. Patients were excluded if the breast cancer diagnosis or intracranial metastatic involvement could not be confirmed, or if no GKRS-

treated lesion could be identified on pretreatment MRI. At the lesion level, the cohort was restricted to lesions treated during the index GKRS course for which a corresponding baseline lesion record was available. Previous whole-brain radiotherapy and intracranial surgery were permitted. Patients and lesions were retained in the source cohort irrespective of the availability of a complete 12-month local-control assessment or complete dose and covariate data; eligibility for individual analyses was determined according to the availability of the relevant endpoint and variables. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of West China Hospital, Sichuan University, on 6 August 2026 (approval No. 2026 Review No. 1838). The requirement for written informed consent was waived because of the retrospective design and the use of de-identified clinical and imaging data, and the approval covered the publication of anonymized MRI images. The final cohort comprised 80 patients, 182 GKRS-treated lesions, and 819 longitudinal MRI records. Lesions constituted the unit of local-control and trajectory analyses, with unique study identifiers used to maintain patient–lesion linkage and account for within-patient clustering.

2.2. GKRS and Dose Variables

Treatments were delivered using Gamma Knife Icon and planned in Leksell GammaPlan version 11.1.1. Contrast-enhanced T1-weighted MRI was the principal planning sequence; T2-weighted and fluid-attenuated inversion recovery images supported target and edema assessment. Targets were delineated by an experienced Gamma Knife neurosurgeon and reviewed by the institutional team [25]. Session number, margin dose, prescription isodose line, target volume, and dose summaries were extracted from treatment records. Biologically effective dose using an α/β ratio of 10 Gy (BED_{10}) was calculated as the sum across planned sessions of $d(1 + d/10)$, where d was the session-specific dose, assuming sufficient repair between sessions [26, 27]. Equivalent dose in 2-Gy fractions (EQD2) was calculated as $BED_{10}/(1 + 2/10)$. BED_{10} and EQD2 were not entered together because they were deterministic transforms. Lesion-to-target correspondence and derived dose values were reconciled against GammaPlan records. Definitive $BED_{10}/EQD2$ values were unavailable for four lesions, including one with unresolved lesion-to-target dose mapping; these values were treated as missing in dose-dependent analyses.

2.3. MRI and Segmentation

Pretreatment MRI was acquired on a 3.0-T GE SIGNA Premier scanner. Contrast-enhanced T1-weighted MRI used gadopentetate dimeglumine 0.1 mmol/kg and approximately 1.4-mm slice thickness; T2-FLAIR used 3-mm slice thickness when available. Images were converted from Digital Imaging and Communications in Medicine (DICOM) to Nearly Raw Raster Data (NRRD), corrected with N4 bias-field correction, resampled to 1-mm isotropic voxels, and intensity normalized. Whole tumor (WT), enhancing tumor (ET), and non-enhancing/necrotic tumor (NET) were manually delineated as separate compartments when available, peritumoral edema was recorded as a qualitative baseline MRI feature. Segmentations were performed in 3D Slicer by two independent readers with 8 and 7 years of neuro-oncologic imaging experience, reviewed by a senior neurosurgeon with 25 years of experience, and resolved by consensus. WT represented the complete visible tumor on pretreatment contrast-enhanced T1-weighted MRI; ET and NET were delineated independently rather than derived by subtraction.

2.4. Endpoints

LC₁₂m was the prespecified lesion-level endpoint. For lesions without earlier documented failure, status was determined from contrast-enhanced MRI acquired 10–14 months after index GKRS. Earlier qualifying volumetric progression, repeat GKRS, or salvage surgery directed at the index lesion was classified as failure at the earliest qualifying assessment. Volumetric progression was defined as at least a 30% increase from the previous minimum volume, with an additional absolute increase of at least 0.2 cm³ for lesions with a baseline volume below 1 cm³ [20, 21]. Unresolved progression versus treatment effect and inadequate follow-up were coded as missing. Longitudinal response phenotype was analyzed separately and did not redefine LC₁₂m. MRI records were linked by unique study identifier and lesion number; a treated lesion no longer visible at follow-up was assigned a volume of zero, whereas a new lesion number represented a new intracranial metastasis. Phenotype classification used 819 records from 154 lesions in 67 patients; longitudinal plots used the core serial dataset of 765 records from 130 lesions in 54 patients. Latest-observed phenotypes were assigned sequentially as complete response/disappearance for non-visibility or zero volume, partial regression for relative volume change $\leq -65\%$, progression for change $\geq +73\%$, and stable control for changes between these thresholds. The 65% reduction and 73% increase thresholds approximate the spherical-volume equivalents of a 30% diameter decrease and a 20% diameter increase, respectively.

2.5. Statistical Analysis

Continuous variables were summarized as medians and interquartile ranges and categorical variables as counts and percentages. Variable-specific denominators were used for missing retrospective data, and missing outcomes were not imputed. Analyses were performed in Python 3.13.9. The primary LC₁₂m analysis used Bayesian mixed-effects logistic regression with a patient-level random intercept and three prespecified fixed effects: $\ln[1 + \text{baseline WT volume (cm}^3\text{)}]$, qualitative edema, and BED₁₀ per 10 Gy. The model was fitted in statsmodels 0.14.5 using BinomialBayesMixedGLM. Default zero-mean Gaussian priors were used for fixed effects (standard deviation 2) and log standard deviations of variance components (standard deviation 1). Odds ratios and 95% posterior credible intervals were reported. A same-covariate binomial generalized estimating equation (GEE) with exchangeable working correlation, patient clustering, and robust covariance was used as a sensitivity analysis. BED₁₀ distributions were compared using a two-sided Mann–Whitney U test. Dose response was further examined using volume-adjusted binomial models with patient-cluster-robust covariance, comparing a linear BED₁₀ term with a four-knot restricted cubic spline at the 5th, 35th, 65th, and 95th percentiles. Model fit was compared using a likelihood-ratio test, Akaike information criterion, and Bayesian information criterion; EQD2 substitution was examined as a sensitivity analysis. Global phenotype comparisons used unrestricted lesion-level permutation tests. The phenotype–LC₁₂m association was summarized using Pearson's χ^2 and Cramér's V and further evaluated using patient-clustered binomial GEE for progression versus non-progression. Patient-level cluster bootstrap resampling with 5,000 replicates provided intervals for Cramér's V and classification measures. A GEE restricted to phenotypes assigned within 10–14 months

assessed timing sensitivity. Systemic therapy was summarized descriptively. All frequentist tests were two-sided.

3. Results

3.1. Cohort and Endpoint Availability

The cohort included 80 patients and 182 treated lesions (Fig. 1). Dose was available for 178 lesions, LC₁₂m for 103, both dose and LC₁₂m for 100, and longitudinal phenotype for 154. Among LC₁₂m-evaluable lesions, 69 were controlled and 34 failed. Of the 79 non-evaluable lesions, 25 lacked adequate assessment because of death, seven had no qualifying MRI within the 10–14-month window, two had insufficient follow-up imaging, and 45 had no specific reason documented in the analytic records. Evaluable and non-evaluable lesions differed in edema, first-session margin dose, previous intracranial surgery, and molecular subtype (**Online Resource 1, Table S1**). Baseline patient, lesion, and treatment characteristics are summarized in Table 1 using variable-specific denominators.

Table 1
Baseline characteristics of the final locked cohort and GKRS-treated lesions.

Characteristic	Overall
Panel A. Patient-level characteristics (N = 80)	
Age at GKRS, years	53 (43–59)
Karnofsky Performance Status, n = 54	90 (80–100)
Female sex	80/80 (100%)
Baseline brain metastasis count	2 (1–4)
Molecular subtype, n/N (%)	
HER2-positive	27/54 (50.0%)
Luminal B	19/54 (35.2%)
Triple-negative breast cancer	8/54 (14.8%)
Pathological receptor information, n/N (%)	
Hormone receptor-positive	19/52 (36.5%)
HER2 IHC 3+	31/52 (59.6%)
Extracranial metastasis	39/54 (72.2%)
Prior whole-brain radiotherapy	13/54 (24.1%)
Prior intracranial surgery	15/54 (27.8%)
Panel B. Lesion- and treatment-level characteristics (N = 182)	
Baseline whole-tumor volume, cm ³	0.38 (0.13–1.53)
Baseline enhancing-tumor volume, cm ³ , n = 169	0.38 (0.13–1.36)
Non-enhancing/necrotic component present	58/182 (31.9%)
Qualitative peritumoral edema present	73/130 (56.2%)
Intracranial hemorrhage present	7/130 (5.4%)
Lesion location, n/N (%)	
Supratentorial	88/130 (67.7%)
Infratentorial	41/130 (31.5%)
Brainstem	1/130 (0.8%)
First-session margin dose, Gy	13 (12–18)

Characteristic	Overall
Panel A. Patient-level characteristics (N = 80)	
First-session prescription isodose line, %	45 (45–50)
BED ₁₀ , Gy, n = 178	60.55 (49.09–85.16)
EQD2 ($\alpha/\beta = 10$ Gy), Gy, n = 178	50.46 (40.91–70.97)

Values are presented as median (interquartile range) or n/N (%). For variables with missing data, denominators are shown in the row label or directly as n/N. All 80 patients and 182 treated lesions were retained in the final locked cohort; smaller denominators reflect missing retrospective documentation rather than additional selection. BED₁₀, biologically effective dose using $\alpha/\beta = 10$ Gy; EQD2, equivalent dose in 2-Gy fractions; GKRS, Gamma Knife radiosurgery; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry.

3.2. Local Control and Dose

The dose-complete primary analysis included 100 lesions from 46 patients and 33 local failures. In the Bayesian mixed-effects model, larger baseline WT volume (OR 1.840, 95% CrI 1.034–3.275) and edema (OR 2.201, 95% CrI 1.062–4.564) were associated with higher odds of failure, whereas higher BED₁₀ was inversely associated (OR per 10 Gy 0.756, 95% CrI 0.699–0.818; Fig. 2). Patient-clustered GEE estimates had the same directions but were less precise: OR 1.482 (95% CI 0.665–3.303) for WT volume, OR 1.519 (95% CI 0.737–3.128) for edema, and OR 0.867 (95% CI 0.701–1.072) per 10-Gy BED₁₀ increase (**Online Resource 1, Table S2**). Median BED₁₀ was higher in controlled than failed lesions (76.18 [IQR 56.84–112.08] vs 53.89 [41.92–73.80] Gy; Mann–Whitney U = 1573; $p < 0.001$). In the volume-adjusted linear model, the BED₁₀ association was attenuated (OR per 10 Gy 0.851, 95% CI 0.659–1.099; $p = 0.215$). A restricted cubic spline improved likelihood relative to the linear model ($\chi^2 = 8.621$; $df = 2$; $p = 0.013$), with lower AIC but similar BIC. This exploratory analysis did not establish a clinically actionable dose threshold; EQD2 produced a similar pattern (**Online Resource 1, Table S3**).

3.3. Longitudinal MRI Response Phenotypes and Local-Control Concordance

Among 154 trajectory-evaluable lesions, 24 (15.6%) showed complete response/disappearance, 59 (38.3%) partial regression, 44 (28.6%) stable control, and 27 (17.5%) progression (Fig. 3). Phenotypes differed in baseline WT volume ($p < 0.001$) and edema ($p = 0.018$), but not in corrected BED₁₀ (permutation $p = 0.173$; **Online Resource 1, Table S3**). In the patient-clustered GEE, WT volume, edema, and BED₁₀ were not independently associated with progression phenotype. Among 103 lesions with both phenotype and LC_{12m} assessment, phenotype and local control were strongly associated (Pearson $\chi^2 = 50.989$; permutation $p < 0.001$; Cramér's V = 0.704; Fig. 4). Progression remained associated with local failure after patient clustering (OR 27.08, 95% CI 7.11–103.20; $p < 0.001$; **Online Resource 1, Table S4**).

Of these lesions, 97 were classified within 10–14 months; restriction to this group yielded a similar association (OR 19.37, 95% CI 5.00–75.09; $p < 0.001$; **Online Resource 1, Table S5**). Progression phenotype identified local failure with 58.8% sensitivity, 97.1% specificity, 90.9% positive predictive value, and 82.7% negative predictive value (**Online Resource 1, Table S4**).

4. Discussion

This study demonstrates that serial volumetric MRI can organize heterogeneous lesion-level responses after GKRS for BCBM into four clinically interpretable phenotypes. Progression phenotype showed strong concordance with LC_{12m} and remained strongly associated with local failure after accounting for within-patient clustering and assessment timing. Baseline whole-tumor volume, qualitative edema, and corrected BED_{10} provided complementary information on local-failure risk in the prespecified Bayesian model. Together, these findings link baseline imaging characteristics, biological dose, and post-treatment MRI evolution within an integrated lesion-level response-assessment framework.

The association of larger baseline WT volume with local failure is consistent with breast-cancer-specific and broader SRS literature [13, 14, 18, 19]. Larger lesions may exhibit greater tissue heterogeneity and planning complexity and may receive lower prescription doses because of normal-tissue constraints. Edema may mark a more adverse local imaging phenotype through blood–brain barrier disruption, vascular permeability, inflammation, or its relationship with lesion size. A recent meta-analysis similarly associated pretreatment perilesional edema with local failure after SRS [28]. The directionally similar estimates across the primary and sensitivity models support further evaluation of WT volume and edema as contextual imaging features after GKRS.

Higher BED_{10} was inversely associated with local failure in the prespecified Bayesian model, although estimates were attenuated in the GEE and conventional volume-adjusted analyses. This pattern is clinically plausible because dose prescription is influenced by lesion size and anatomical constraints, and previous studies emphasize the joint effects of target size, fractionation, and toxicity [17–19]. The exploratory spline analysis suggested a nonlinear dose–response relationship but did not define a clinically actionable threshold. These results support interpreting biological dose in conjunction with lesion burden rather than applying a universal escalation rule [26, 27]. Preliminary prospective data from the SAFER study also support a BED_{10} –local-control relationship, although its population, dose model, and follow-up differed from those of the present study [29].

The longitudinal phenotype analysis extends binary local-control assessment by retaining clinically recognizable patterns of disappearance, regression, stability, and enlargement. The association between progression phenotype and LC_{12m} persisted after patient-level clustering and restriction to the 10–14-month assessment window. Its high specificity and positive predictive value suggest that progression phenotype may provide an informative rule-in signal during surveillance. This framework is intended to describe lesion evolution alongside formal local-control assessment, particularly when post-SRS enlargement may reflect progression, radiation injury, or mixed treatment effects [23]. Longitudinal brain-

metastasis imaging resources likewise demonstrate the value of serially annotated MRI for standardized assessment and method development [30]. Prospective studies with standardized imaging intervals and repeated volumetric measurements are needed to evaluate its clinical utility.

This retrospective single-center study had limited local-failure events, and LC_{12m} was evaluable in 103 of 182 lesions, creating potential follow-up selection bias. Longitudinal phenotypes were based on latest-observed MRI; complete salvage timing and follow-up volumetry metadata were unavailable for all lesions, and radiation necrosis was not uniformly confirmed. Bayesian effect magnitudes were model-dependent, although directions were preserved in the same-covariate GEE. Although the original permutation analysis was lesion-level, the phenotype–LC association remained strong in patient-clustered GEE, cluster-bootstrap, and 10–14-month sensitivity analyses. Systemic therapy was heterogeneous and incompletely time-resolved and was therefore summarized descriptively rather than modeled as a causal treatment exposure (**Online Resource 1, Table S6**). External validation remains necessary.

5. Conclusions

Longitudinal volumetric MRI phenotypes provide a clinically interpretable lesion-level framework for characterizing response after GKRS in patients with BCBM. Progression phenotype remained strongly associated with local failure after patient clustering and within the prespecified 10–14-month imaging window, supporting its value as an informative signal during post-treatment surveillance. Baseline whole-tumor volume, peritumoral edema, and corrected BED₁₀ provided complementary information on local-failure risk. Together, these findings integrate pretreatment imaging, biological dose, and post-treatment MRI evolution and support further evaluation of standardized longitudinal response assessment after GKRS.

Declarations

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Biomedical Ethics Review Committee of West China Hospital, Sichuan University, on 6 August 2026 (approval No. 2026 Review No. 1838).

Consent to Participate

The requirement for written informed consent was waived by the Ethics Committee of West China Hospital, Sichuan University, because of the retrospective design and the use of de-identified clinical and imaging data.

Consent for Publication

The Ethics Committee of West China Hospital, Sichuan University, approved the publication of fully anonymized MRI images and waived the requirement for specific consent for publication.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Author Contribution

Conceptualization, S.D. and J.C.; methodology, S.D. and J.C.; investigation, S.D., T.H., and Z.L.; data curation, S.D., T.H., and Z.L.; formal analysis, S.D.; validation, S.D., T.H., and Z.L.; writing—original draft preparation, S.D.; writing—review and editing, S.Z., F.L., X.L., H.L., and J.C.; supervision, J.C. All authors read and approved the final manuscript.

Data Availability

The datasets generated and analyzed during the current study are not publicly available because they contain institutional clinical, imaging, and treatment-planning data. De-identified data may be available from the corresponding author upon reasonable request and subject to institutional approval.

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Figures

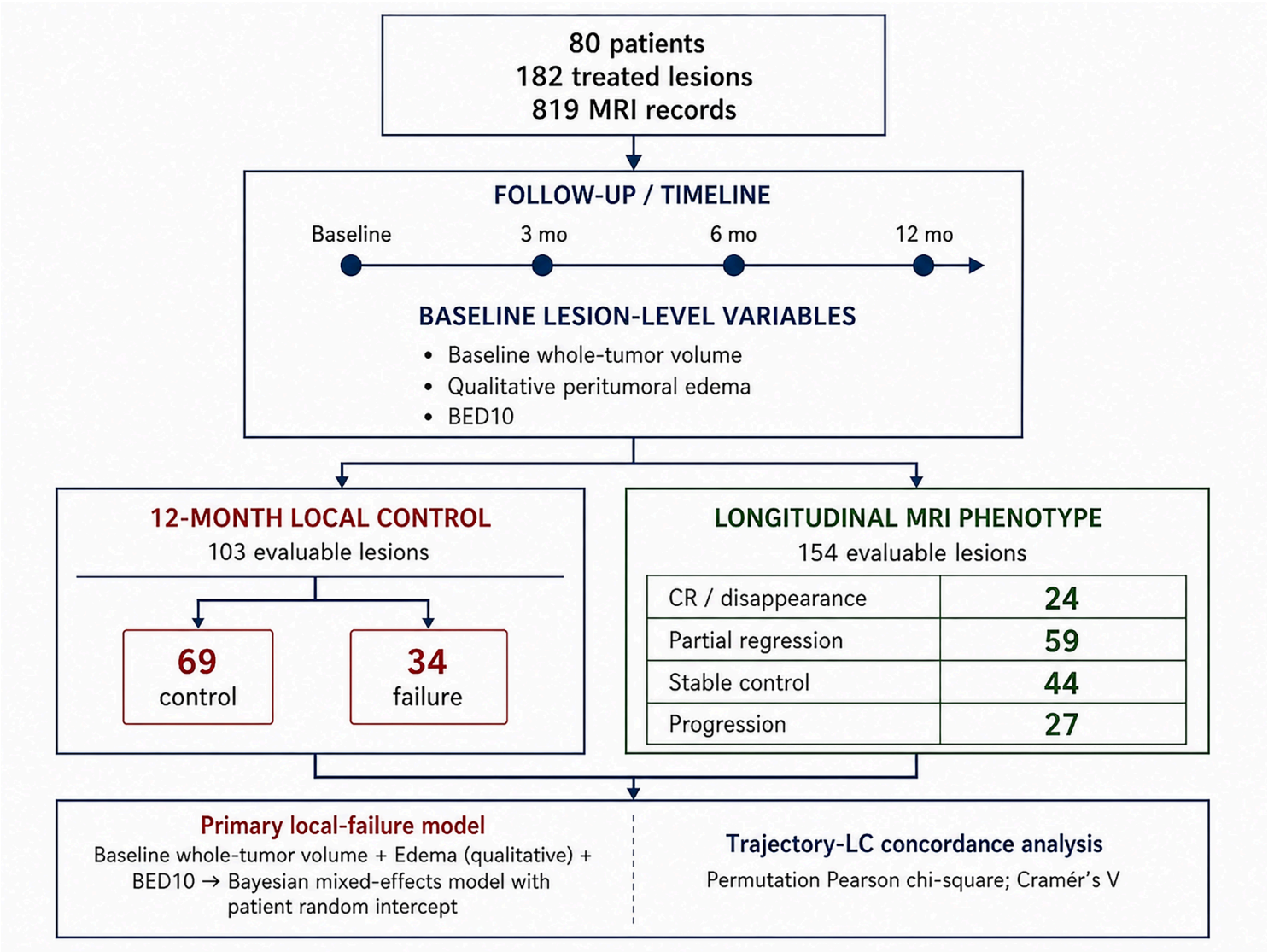


Figure 1

Study overview and lesion-level analytical framework. The institutional cohort included 80 patients, 182 GKRS-treated lesions, and 819 longitudinal MRI records. Serial contrast-enhanced MRI examinations were linked while retaining lesion identity across follow-up. The 12-month local-control assessment used a 10–14-month window and included 103 lesions, whereas 154 lesions were evaluable for longitudinal MRI phenotype. The primary mixed-effects model evaluated baseline WT volume, peritumoral edema, and BED₁₀. BCBM, breast cancer brain metastases; BED₁₀, biologically effective dose using an α/β ratio of 10 Gy; CR, complete response; GKRS, Gamma Knife radiosurgery; LC, local control; MRI, magnetic resonance imaging; mo, months; WT, whole tumor.

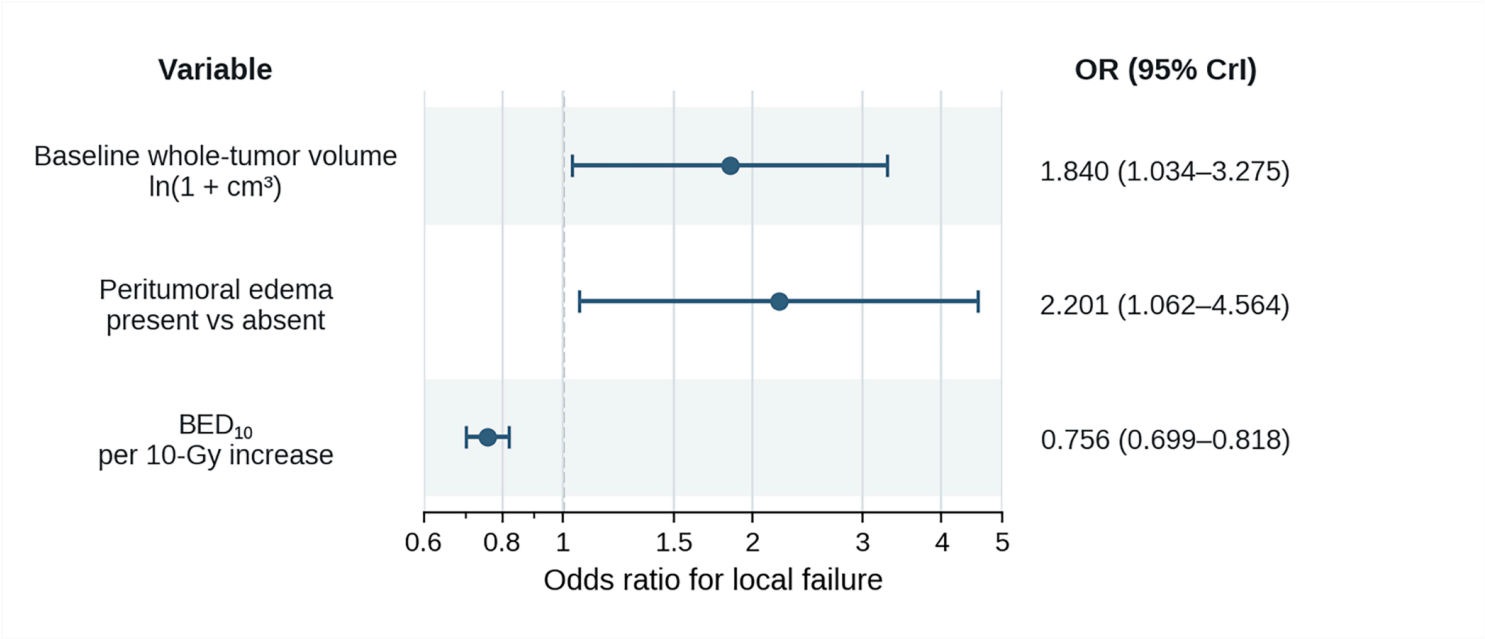


Figure 2

Factors associated with local failure after GKRS. Odds ratios and 95% posterior credible intervals are shown for the three prespecified fixed effects in the dose-reconciled primary Bayesian mixed-effects logistic regression model with a patient-level random intercept. The analysis included 100 lesions from 46 patients and 33 local failures. A same-covariate patient-clustered GEE sensitivity analysis is reported in **Online Resource 1, Table S2**. BED₁₀, biologically effective dose calculated using an α/β ratio of 10 Gy; CrI, credible interval; GKRS, Gamma Knife radiosurgery; OR, odds ratio.

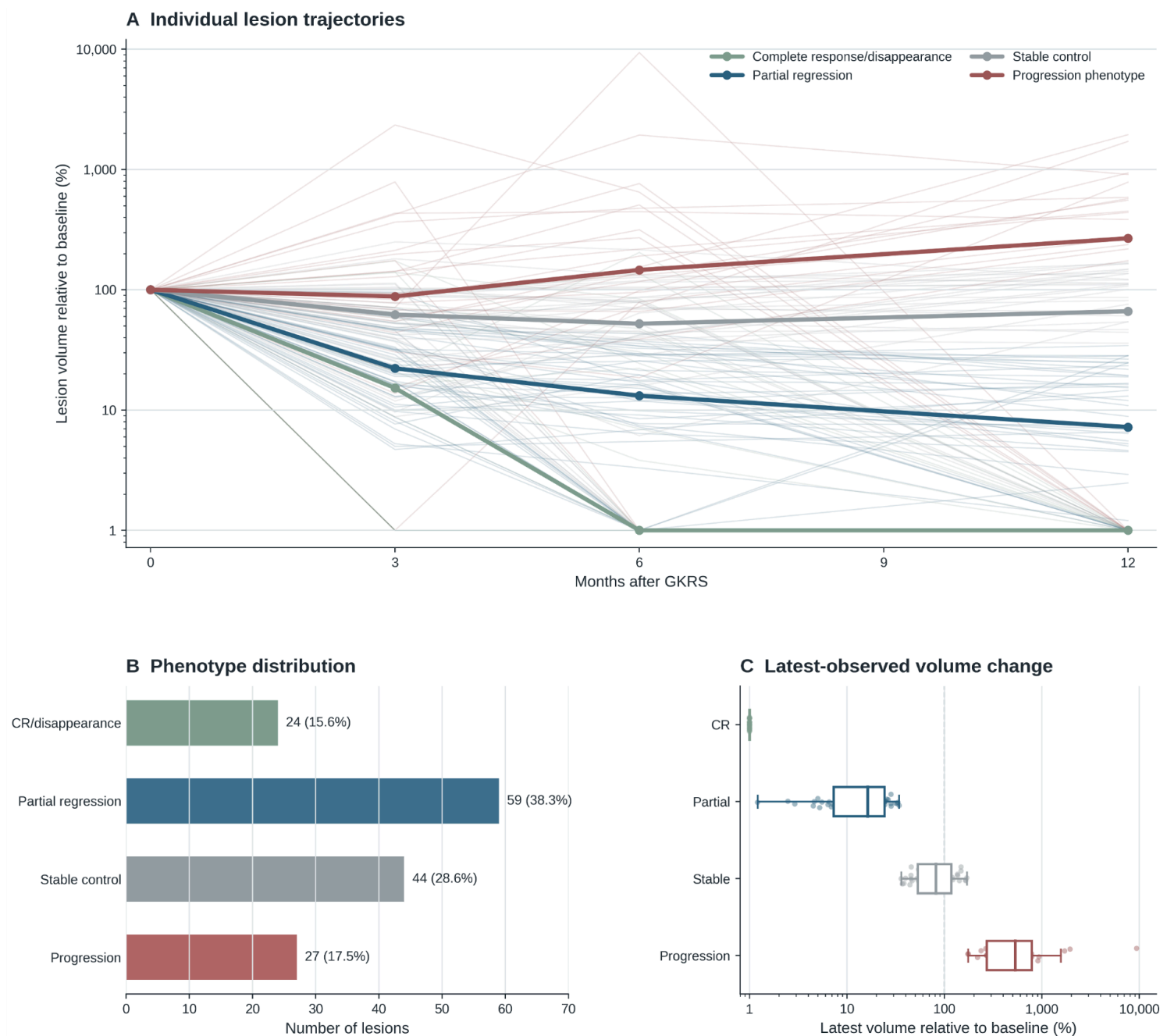


Figure 3

Longitudinal MRI response phenotypes after GKRS. (A) Individual lesion trajectories in the 130-lesion core serial volumetric dataset are shown as volume relative to baseline across available follow-up time points; thick lines represent phenotype-specific medians at each scheduled time point. Zero-volume observations are displayed at 1% to permit logarithmic scaling. (B) Distribution of the four latest-observed volumetric phenotypes among all 154 trajectory-evaluable lesions after supplementary inclusion. (C) Latest-observed lesion volume relative to baseline in the 130-lesion core serial volumetric dataset; boxes show the median and interquartile range. These phenotypes are descriptive and are not presented as surrogate endpoints. CR, complete response; GKRS, Gamma Knife radiosurgery; MRI, magnetic resonance imaging.

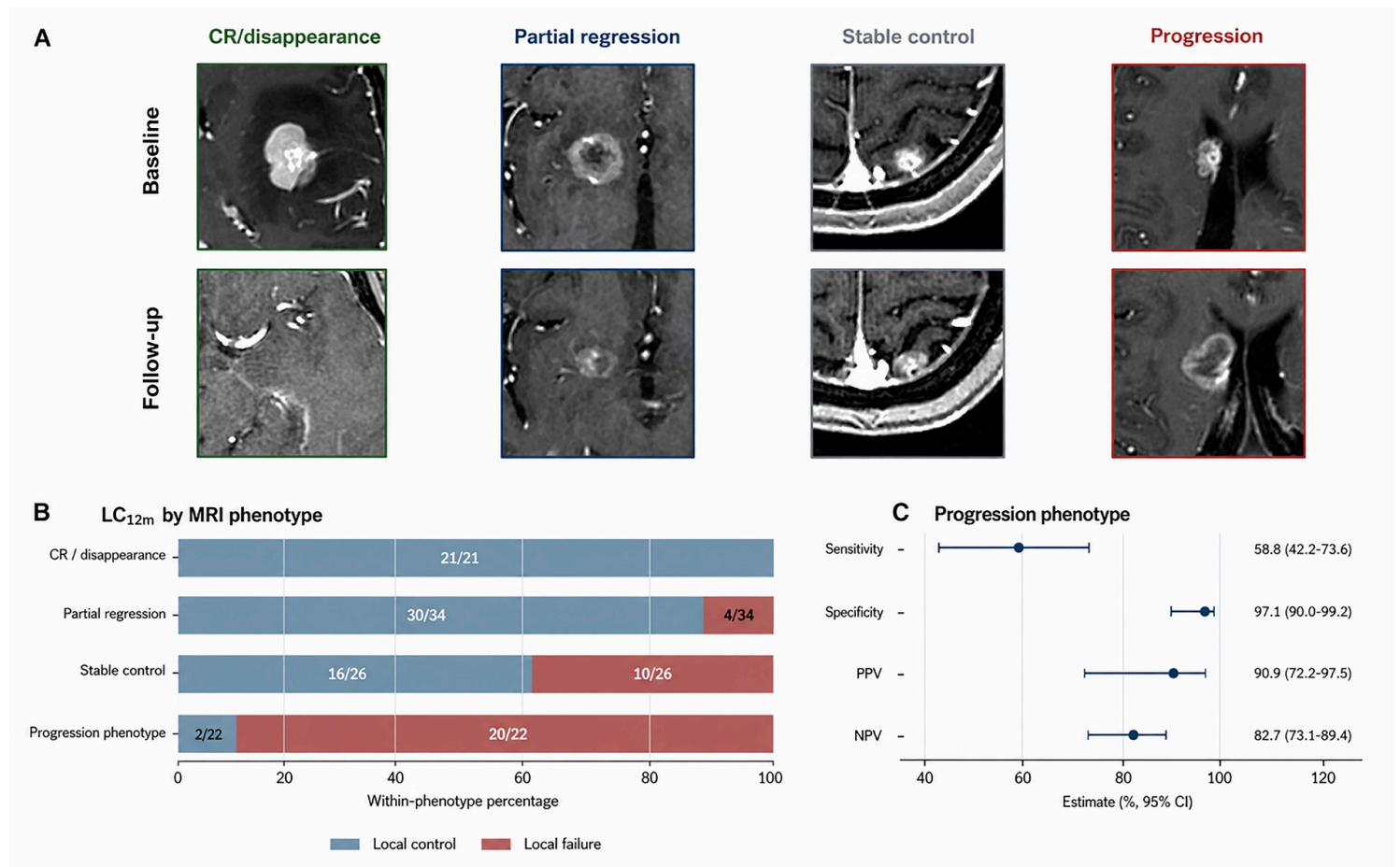


Figure 4

Representative longitudinal MRI patterns and concordance with 12-month local control. (A) Baseline and follow-up contrast-enhanced T1-weighted MRI examples of complete response/disappearance, partial regression, stable control, and progression phenotype. The illustrated follow-up intervals were 11.24 months for complete response/disappearance, 7.43 months for partial regression, and 12.0 months for stable control and progression. (B) Within-phenotype proportions of local control and local failure among 103 lesions with both assessments. The original association was evaluated using 20,000 unrestricted lesion-level label permutations ($p < 0.001$; Cramér's $V = 0.704$). Patient-clustered GEE and cluster-bootstrap sensitivity analyses are reported in **Online Resource 1, Table S4**; the analysis restricted to phenotype classifications within 10–14 months is reported in **Online Resource 1, Table S5**. (C) Sensitivity, specificity, positive predictive value, and negative predictive value of progression phenotype for local failure. CI, confidence interval; CR, complete response; LC_{12m}, 12-month local control; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value.

Supplementary Files

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- [Supplementarymaterialsjno.docx](#)