

Radiation Necrosis Following Stereotactic Radiosurgery: Incidence, Risk Factors, Imaging, and Management

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Executive Summary

- **Incidence:** Radiation necrosis (RN) is a common late complication of intracranial stereotactic radiosurgery (SRS), with reported rates ranging **2–30+%** depending on tumor type, dose, and follow-up. For brain metastases, landmark studies report RN in ~8–11% at 1–2 years (RTOG-9005), ~24–26% in early series, and ~5% in modern trials. For benign tumors, meningioma cohorts show RN rates ~3–27% and vestibular schwannoma ~0.5–12%. Fractionated SRS markedly lowers RN incidence for larger lesions.
- **Risk Factors:** Key predictors include *treatment-related* factors (high dose per fraction, large treated volume [especially normal brain V10–V12], re-irradiation) and *patient/tumor* factors (tumor size, histology, location, concurrent therapies). E.g. normal brain V12 of 5/10/15 cc yields ~10/15/20% RN risk. Concurrent systemic therapy or adjuvant resection also elevate risk (adjusted ORs ~8.2 and 3.7). Prior SRS increases RN risk (~20% 1-year RN if same lesion was re-treated).
- **Imaging:** Distinguishing RN from tumor recurrence is challenging. Conventional MRI often shows **ring-enhancement with edema**, but this is nonspecific. Advanced MRI (DWI, perfusion, spectroscopy) and metabolic imaging improve accuracy. DWI/ADC tends to be **higher** in RN. MRI “T1/T2 mismatch” (ill-defined T1 enhancement vs surrounding T2 signal) has ~83% sensitivity/91% specificity. Perfusion MRI is useful: e.g. relative cerebral blood volume (rCBV) cutoff ~1.5–2.1 distinguishes tumor vs RN (sensitivity ~91–100%, specificity ~72–95%). MR spectroscopy (low Cho/Cr ratio suggests RN). Amino-acid PET tracers (e.g. ¹⁸F-FET, ¹⁸F-FDOPA) outperform FDG; for instance, F-DOPA PET can reach ~90% sensitivity/specificity at optimized uptake thresholds. No single modality is definitive; a **multimodal approach** (MRI + perfusion + PET) yields best diagnostic accuracy.
- **Management:** First-line therapy for symptomatic RN is **corticosteroids** (rapid edema control). However, prolonged steroids have toxicity. **Bevacizumab** (anti-VEGF) is highly effective: a meta-analysis reported symptomatic improvement in ~88% of patients, radiographic improvement in ~86%, and steroid reduction in ~45%. Typical regimens are 5–10 mg/kg IV every 2–3 weeks for 4–6 cycles, which often yields dramatic edema resolution, though recurrence after discontinuation can occur. **Laser interstitial thermal therapy (LITT)** is a minimally invasive option for RN (often concurrently obtaining biopsy); it yields symptomatic control in ~71% (vs ~88% with bevacizumab) and radiographic improvement ~65% (vs 86%), with similar safety profiles. **Surgical resection** is reserved for large, refractory RN causing mass effect, and yields rapid relief of symptoms and allows tissue diagnosis (histology often shows mix of gliosis, necrosis, or occult tumor). **Hyperbaric oxygen** has anecdotal support (angiogenesis/edema reduction) but lacks high-level evidence. **Follow-up:** Close MRI surveillance (NCCN: every 2–3 months for 1–2 years then 4–6 months) is recommended to identify RN and recurrences early.

Abstract

Objective: To comprehensively review the incidence, risk factors, diagnostic imaging, and management of radiation necrosis (RN) after stereotactic radiosurgery (SRS). **Methods:** We performed a structured literature search of PubMed, Embase, and major oncology/radiology journals (2015–2025) for studies on RN after cranial SRS. We synthesized data on RN incidence by tumor type and SRS parameters, predictive factors (dose-volume metrics, patient/tumor factors), advanced imaging modalities (perfusion MRI, DWI, spectroscopy, amino-acid PET), and treatment outcomes (steroids, bevacizumab, surgery, LITT, etc). Data from meta-analyses, prospective trials, and consensus guidelines were prioritized. **Results:** Reported RN rates vary widely. In brain metastases, early trials (RTOG) reported ~8–11% at 2 years, institutional series up to 25–30%, whereas modern radiosurgery trials report lower rates (~5%). Benign tumors show RN in ~3–27% (meningiomas) and ~0.5–12% (vestibular schwannomas) depending on size and dose. High single-fraction dose and large treatment volumes strongly predict RN; for example, normal brain V12 of 5, 10, >15 cc correspond to ~10%, 15%, 20% symptomatic RN risk. Fractionated SRS (3–5 fractions) markedly reduces RN for larger lesions. Concurrent therapies (chemotherapy, immune therapy) and re-irradiation also increase RN risk. Imaging: Conventional MRI is nonspecific (RN and tumor both enhance and have edema). Advanced MRI/perfusion (rCBV, PSR) and MR spectroscopy can help: one series found rCBV cutoff 1.52 yields 91% sensitivity, 72% specificity, and PSR cutoff 76% yields 96%/100%. Amino-acid PET (FET, FDOPA, MET) has high accuracy (~90+% sensitivity/specificity) for RN vs tumor; FDG-PET is less reliable (~75–85% sensitivity). Management: Steroids remain first-line for symptomatic RN. Bevacizumab (7.5–10 mg/kg IV q2–3 weeks for several cycles) leads to clinical and radiographic improvement in ~80–90%. LITT and surgical resection are effective for refractory RN or diagnostic uncertainty. Evidence suggests bevacizumab provides better symptom control than LITT, but choice depends on lesion size/location and patient factors. **Conclusions:** RN after SRS is a common, dose-dependent complication. Risk can be mitigated by respecting V10–V12 constraints and fractionating large treatments. Multimodal imaging is needed to distinguish RN from tumor. Management is multidisciplinary: steroids and bevacizumab are mainstays, with neurosurgery or LITT for selected cases. Recommendations include careful treatment planning (limit V12), vigilant imaging follow-up, and a stepwise approach to therapy (steroids → anti-VEGF → ablative/surgical).

Keywords: Radiation Necrosis, Stereotactic Radiosurgery, Tumors

Introduction

Advances in stereotactic radiosurgery (SRS) have enabled high-dose, highly conformal treatment of intracranial tumors (metastases, AVMs, benign tumors) with excellent local control. However, the high dose per fraction can injure normal brain and lead to radiation necrosis (RN), a pathologic entity characterized by blood-brain barrier disruption, vascular hyalinization, and coagulative necrosis in the irradiated field. RN may manifest months to years after SRS (commonly within 3–12 months), and clinically ranges from asymptomatic radiographic changes to progressive neurological deficits (seizures, focal deficits, cognitive decline). Distinguishing RN from tumor recurrence on imaging is critical as treatments diverge (avoiding unnecessary surgery or re-irradiation for RN). Yet, no single imaging modality definitively differentiates RN from active tumor. In this article, we review the latest evidence (2014–2024) on incidence and risk factors of SRS-related RN, advanced imaging features and diagnostic accuracy, and management strategies including medical, surgical, and novel interventions. We emphasize quantitative dose-volume predictors (e.g. V12, BED), imaging sensitivity/specificity (DWI, PWI, PET tracers), and outcomes of treatments (steroid courses, bevacizumab protocols, LITT and surgery).

Methods

We conducted a systematic search of PubMed, Cochrane, and Embase through 2025 using terms including “stereotactic radiosurgery”, “radiation necrosis”, “brain metastases”, “incidence”, “V12”, “dose-volume”, “MRI perfusion”, “PET”, “bevacizumab”, “LITT”, “management”. We prioritized recent meta-analyses, prospective trials, large retrospective cohorts, and consensus guidelines. Reference lists of key reviews were scanned for additional sources. Data extracted included RN incidence rates, odds ratios or hazard ratios for predictive factors (age, tumor size/location, V10/12 volumes, fractionation), sensitivity/specificity of imaging tests, and treatment response rates. Where possible, quantitative results (e.g. AUC, thresholds) were recorded. Findings were synthesized narratively and summarized in tables and figures.

Results

Incidence and Timing of Radiation Necrosis

Reported RN rates vary widely due to heterogeneous definitions and follow-up durations. In early SRS series of brain metastases, Neurological Oncology Group (RTOG-9005) reported 8% RN at 1 year and 11% at 2 years. Two large series found even higher rates: an Italian cohort (310 lesions) found 24% RN (10% symptomatic), and

MSKCC (271 lesions) reported 26% RN (17% symptomatic) at ~17 months follow-up. In contrast, a modern randomized trial (SRS ± WBRT in 1–3 metastases) observed only 4.5% RN in the SRS arm, reflecting differences in volume and dose constraints. In cumulative data, RN incidence for brain metastases is often cited as ~5–15%; very large series suggest ~8%–12% by 1–2 years on average.

For benign tumors, RN incidence depends on histology. Recent meta-analysis: meningiomas treated with SRS have RN in ~3.3% to 26.8%, whereas vestibular schwannomas show ~0.5%–12%. Demetz et al. (2023) found 15.6% RN in an Innsbruck cohort of benign tumors (skull-base predominance). AVMs have lower RN risk compared to metastases for a given V12, due to different tissue tolerances. Overall, RN typically appears between 3–12 months post-SRS, though late presentations up to 3–5 years are reported.

Table 1 (below) summarizes RN incidence by study and tumor type. Risk increases with longer follow-up and more sensitive imaging detection.

Study (year)	Tumor Type	SRS Type	RN Incidence
Chao et al. (2024)	Brain metastases	Single-fraction	8% (1y), 11% (2y) (RTOG9005); 24% (Italian series, 10% symptomatic); 26% (MSKCC series, 17% symptomatic); 4.5% (5–10y trial, SRS alone)
Neslihan Gecici et al. (2024)	CNS neoplasms (mixed)	SRS/Hypofraction	RN overall 2–46% (literature range)
Demetz et al. (2023)	Benign tumors (meningioma, VS, etc.)	Single-fraction	RN overall 15.6%; Meningioma: 3.3–26.8%; VS: 0.5–12%
Milano et al. (2021)	Metastases/AVM	Single/Multi	For metastases: 10% RN at V12=5cc, 15% at 10cc, 20% at >15cc; AVM somewhat lower.

Predictive Factors for RN

Treatment-Related Factors

- **Dose and volume metrics:** Consistently, higher dose and larger irradiated volume are dominant predictors. The normal brain volume receiving ≥ 12 Gy (V12) strongly correlates with RN risk. For single-fraction SRS to metastases, V12 of 5, 10, 15 cc corresponded to ~10%, 15%, and 20% symptomatic RN risk. Another analysis found symptomatic RN >50% when V12 >10 cc. A practical guideline: aim for V12 < 8–10 cc if possible. Hypofractionation (e.g., 3–5 fractions) allows larger target volumes; HyTEC data suggest for 3 fractions (delivering ~25–30 Gy total), brain+target V20 <20 cc limits necrosis risk <10%.
- **Dose per fraction and total dose:** Higher single-fraction doses increase RN. RTOG-9005 indicated recommended limits (24 Gy for ≤ 2 cm lesions, 18 Gy for 2.1–3cm, 15 Gy for 3.1–4cm) to keep RN <10%. Boosts or hotspots (>110% of dose in target) also raise risk.
- **Fractionation:** Fractionated SRS (hypofractionation) reduces RN. HyTEC: V20 Gy (3 fr) <20 cc yields <10% RN, V24 Gy (5 fr) <20 cc yields <10%. Yan et al. (2021) reported 12-month RN 15.6% (symptomatic 7.0%) in 91 patients given salvage 5-fraction SRS, lower than expected for single-fraction boosts.
- **Re-irradiation:** Prior radiation markedly ups RN risk. Sneed et al.: same-lesion re-SRS had ~20% 1-year RN risk vs 3% with no prior RT. Even prior WBRT raises risk (4% with prior SRS, 8% with concurrent WBRT).
- **Adjunctive therapies:** Concurrent chemotherapy/immunotherapy may interact. In one series of lung/melanoma mets with immunotherapy, V12 >20cc gave 20% RN vs 6.6% if V12 <12cc. Some chemotoxins (e.g. capecitabine) increase RN risk.

Patient and Tumor Factors

- **Tumor histology:** Certain histologies seem RN-prone. Chao et al. noted lung adenocarcinoma, renal, ALK+/HER2+ breast, and BRAF-mutated melanoma had higher RN in metastases. Low-grade tumors (e.g. meningioma) may tolerate less dose, raising necrosis chance with high dose.

- **Tumor size:** Larger tumors (diameter >1.5–2 cm) incur higher RN risk. Sneed et al.: lesions <1.5 cm had ≤3% RN, whereas ≥1.6 cm had ≥10%. Large size also correlates with larger V12.
- **Location:** Some brain regions are more vulnerable. Occipital/temporal lobes showed slightly higher RN rates. Brainstem lesions are special: cooperative studies (496 patients) found modest RN (<5–10%) for brainstem mets up to 2 cm, but caution is needed due to critical function. Skull-base lesions (meningiomas) had *lower* symptomatic necrosis risk, possibly from smaller V12 in tight anatomical confines.
- **Patient age/comorbidities:** Conflicting data; one study found older age predicted poorer steroid response for RN, but age itself is not a consistent risk factor.
- **Genetics/repair:** Rarely, germline or tumor mutations affecting radiosensitivity (e.g. ALK, ATM) could influence RN, but data are sparse.

Summary: In practice, dosimetric factors (dose, volume, fractionation) are the strongest predictors, while patient/tumor factors are secondary. Limit V12 and consider hypofractionation to mitigate RN risk.

Imaging Features and Diagnostic Modalities

Differentiating RN from tumor recurrence/progression is a core challenge. Conventional MRI findings (enhancing lesion with edema) overlap between RN and tumor. However, some patterns favor RN: “Swiss-cheese” or “soap bubble” enhancement, central necrosis with peripheral enhancement, and widespread T2/FLAIR edema. Nonetheless, MRI alone has poor specificity.

MRI Techniques

- **Contrast-enhanced MRI:** RN typically appears as a ring-enhancing lesion on T1 post-contrast with surrounding T2 hyperintensity (vasogenic edema). But tumor can look identical. Sometimes RN yields poorly defined margins.
- **Diffusion-weighted MRI (DWI/ADC):** RN tends to have higher ADC (less restricted diffusion) than viable tumor. A “lesion quotient” (ratio of non-enhancing T2 to enhancing T1 volume) was proposed but not reproducible. A more robust finding: T1/T2 mismatch (T2 FLAIR extension beyond T1 enhancement) is more common in RN. One series reported T1/T2 mismatch yields ~83% sensitivity and 91% specificity for RN.
- **MR Perfusion:** Measures relative cerebral blood volume (rCBV). Tumor recurrence has high neovascularity (high rCBV) whereas RN does not. Reported cutoffs: e.g. rCBV ≥2.1 was 100% sensitive and 95% specific for tumor. Another study found rCBV >1.52 had 91% sensitivity/72% specificity for tumor. Perfusion is complicated near vessels/air. Signal-recovery (PSR) metrics can also differentiate: one group showed PSR <76% (i.e. poor recovery) had 96% sensitivity, 100% specificity for tumor.
- **MR Spectroscopy:** Measures metabolites (Cho, NAA, Cr, lactate). Tumor recurrence often shows high choline (membrane turnover), whereas RN shows reduced metabolites, elevated lipids/lactate. Thresholds vary; one review noted Cho/Cr <1.0 and Cho/NAA <1.5 favored RN. Meta-analyses report accuracy ~80–90% for MRS in this setting. Combining spectroscopic ratios (e.g. Cho/NAA) and perfusion increases accuracy.
- **Chemical Exchange Saturation Transfer (CEST):** Advanced sequence probing protein content; emerging data suggest ability to distinguish RN, but still investigational.

PET Imaging

- **FDG-PET:** Historically used but limited in brain due to high background. Studies show mixed results. Chao et al.: institutional FDG-PET had ~75% sensitivity/80% specificity. A meta-analysis found pooled ~85% sensitivity/90% specificity, but values vary and overlap is common. Not very specific for small lesions.
- **Amino-Acid PET (MET, FET, FDOPA, FLT):** These tracers are preferred. E.g., ¹⁸F-FET or ¹¹C-MET uptake is high in tumor, low in RN. A pooled analysis found FET PET had ~94% sensitivity, 88% specificity for distinguishing RN. FDOPA-PET studies report ~90–100% sensitivity and 85–100% specificity at optimal SUV or uptake-ratio thresholds. For example, one study found an uptake ratio

cutoff (lesion-to-normal) of 1.59 yielded 90% sens and 92% spec. Newer amino-acid analogs (fluciclovine, DASA-23) show promise with similarly high accuracy.

- **PET perfusion (15O-H₂O) or PET-MR** combinations can add information but are specialized.
- **Advanced MRI+PET fusion:** Studies indicate combining modalities (e.g. MRI perfusion + FET-PET) yields higher diagnostic accuracy (approaching 95% combined).

No imaging is foolproof. In ambiguous cases, short-interval MRI (1–2 months) or multimodal imaging is advised. Ultimately, pathologic confirmation via biopsy/LITT may be needed if imaging is inconclusive and management depends on ruling out tumor.

Diagnostic Performance Table (sample)

Modality	Parameter	Cut-off/ Finding	Sensitivity	Specificity	Reference
DWI (ADC)	Elevated ADC (RN)	–	–	–	Qualitative (RN high ADC)
MRI (T1/T2 mismatch)	T1 enhancement < T2 edema	–	83%	91%	{T1/T2 mismatch} study
DSC-MRI (rCBV)	Mean rCBV tumor vs RN	≥1.52 (tumor)	91%	72%	Barrajas et al.
DSC-MRI (PSR)	Percent signal recov.	≤76% (tumor)	96%	100%	Barrajas et al.
MRS (Cho/NAA)	Metabolite ratio	>2.0 (RN low)	~80%	~85%	Meta-analyses (e.g. Ajnr 2019)
FDG-PET	SUV or uptake	–	~75–85%	~80–90%	Institutional data
MET/FET-PET	Tumor/normal uptake	>1.5–2.0 ratio (tumor)	~90–95%	~85–95%	Meta-analysis
FDOPA-PET	Tumor/normal uptake	~1.4–1.6 ratio	~80–90%	~90–100%	Ceccon et al., JNM 2014

Table 2 (above) compares diagnostic performance; values vary by study.

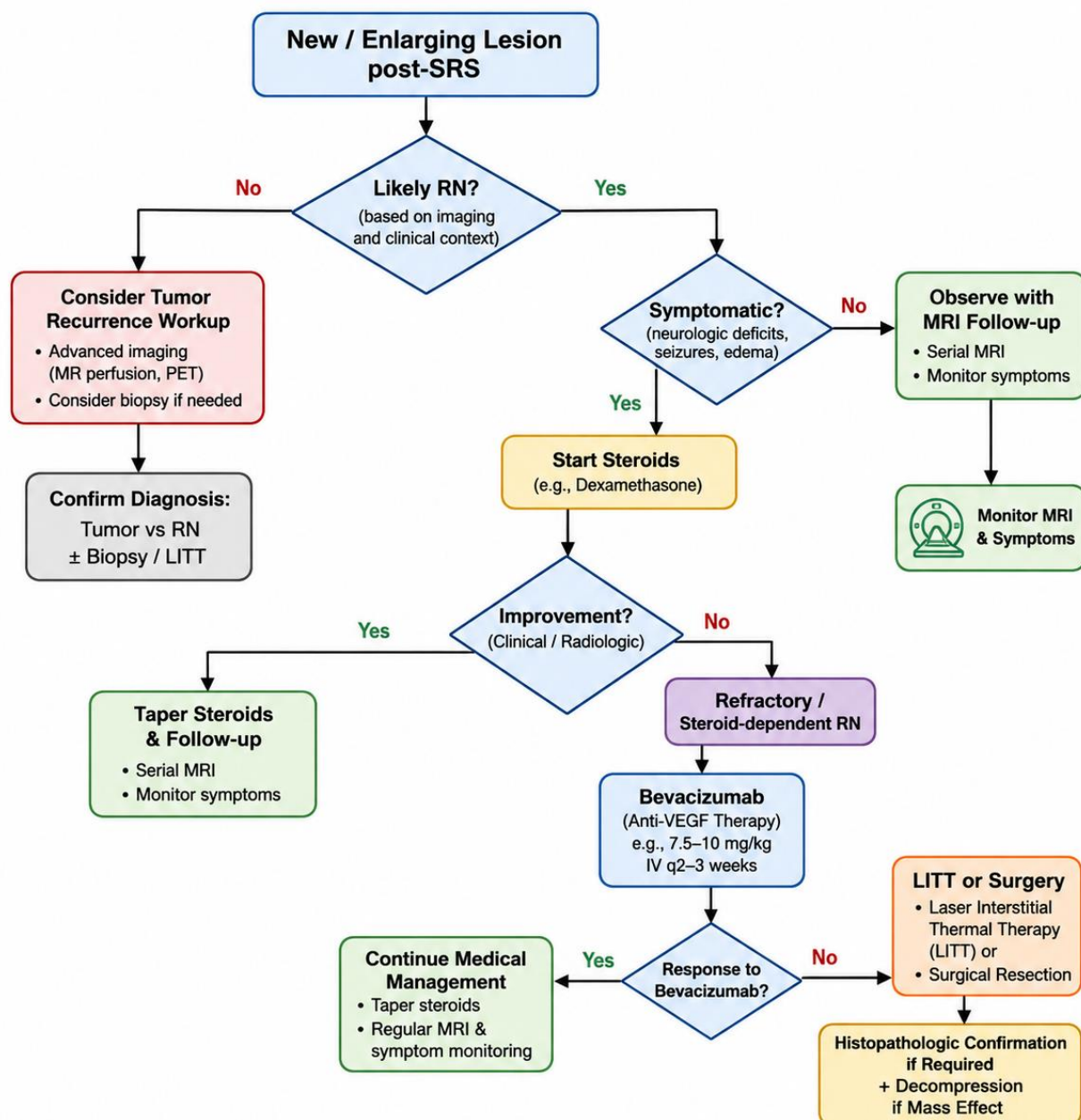
Management Strategies and Outcomes

Medical Management

- **Corticosteroids:** First-line for symptomatic RN. Dexamethasone (4–10 mg daily) rapidly reduces edema and symptoms. Most patients show prompt improvement. In the bevacizumab vs LITT meta-analysis, ~90% in bevacizumab group and 71% in LITT group were on steroids pre-treatment. Steroids have no effect on underlying RN pathology; long-term use leads to dependency, myopathy, immunosuppression, making steroids only a temporizing measure. Current practice: start steroids if significant edema/symptoms, then taper over weeks to minimize side effects.
- **Bevacizumab (anti-VEGF):** Evidence level I (randomized trial). Reduces vascular permeability and edema by neutralizing VEGF from necrotic tissue. Levin et al. (2004) RCT (14 pts) showed all bevacizumab-treated patients had radiographic and neurologic improvement. Meta-analyses report dramatic responses: ~87–88% achieve symptom stability/improvement, ~86% radiographic improvement, and ~40–60% steroid discontinuation. Dosage regimens vary; common practice is 5–10 mg/kg IV every 2–3 weeks for 4–6 cycles (some protocols give 4 cycles and assess). Lower doses (5 mg/kg) can suffice in many cases. Adverse events are usually grade 1–2 (hypertension, proteinuria); serious events (thrombosis, hemorrhage) are <5%. Sustained benefit may require maintenance or repeat infusions, as RN can recur after stopping.
- **Anticoagulation/Antiplatelets:** Hypothesized to help microthrombi; no strong evidence supports routine use. Studies are limited; some clinicians use aspirin or enoxaparin anecdotally, but NCCN does not list anticoagulation.
- **Other medications:** Hyperbaric oxygen (HBOT) has been tried to improve hypoxia and promote angiogenesis. Small series report clinical/radiographic stabilization in many cases. Pentoxifylline/clodronate and vitamin E (as in diffuse brain radiation injury) have no specific data in SRS-RN.

Surgical and Interventional Approaches

- **Surgical resection:** Indicated for large, symptomatic RN refractory to medical therapy or when diagnosis is uncertain. Benefits: immediate mass effect relief, tissue diagnosis. Outcomes: surgery often yields rapid clinical improvement; pathology may reveal pure necrosis, pure tumor, or mixed. Morris et al. (J Neurosurg 2015) reported good outcomes with resection of RN (though sample is mixed with tumors). Risks: neurosurgical complications (infection, deficits) plus recurrence if underlying tumor exists. Surgery is often considered when lesion is >3–4 cm, causing significant edema/herniation, or when biopsy is needed.
- **Laser Interstitial Thermal Therapy (LITT):** MRI-guided laser ablation via a burr hole. Often used for deep or surgically challenging lesions, and can obtain pathology. Case series show ~70–80% symptomatic improvement and >60% radiographic control. In meta-analysis, 71.2% of patients had symptom control with LITT vs 87.7% with bevacizumab; radiographic stabilization was 64.7% (LITT) vs 86.2% (bevacizumab). Typical protocol: 10–15 W laser, ablation of contrast-enhancing rim. Transient swelling post-LITT can worsen symptoms initially. Adverse: hemorrhage, edema. LITT allows biopsy but is more invasive than medical therapy. No randomized trials; choice is individualized by lesion location and patient factors.
- **Flowchart of Management:**



(Figure 1) A conceptual management algorithm: if imaging and clinical context favor RN (vs tumor), assess symptoms. For symptomatic RN, begin corticosteroids. If no improvement or steroid dependence, add bevacizumab. Refractory cases may require LITT or resection. Asymptomatic RN can often be observed with serial MRI. Biopsy/LITT is considered when diagnosis is uncertain.

Outcomes and Complications

- **Steroid outcomes:** Most patients respond (headache/edema relief); however ~30–40% require long courses. Chronic use leads to complications (diabetes, osteoporosis, infection, myopathy) so alternatives are sought.
- **Bevacizumab outcomes:** Meta-analysis (Gecici 2024) indicated bevacizumab (n=210) achieved symptom control in 87.7% and radiographic control in 86.2%. Steroid discontinuation (~45%) was similar between bevacizumab and LITT groups. Adverse events were low-grade in >70%.

- **LITT outcomes:** Symptomatic improvement in 71.2%, radiographic control 64.7%. If combined with biopsy, provides pathology.
- **Surgery outcomes:** High symptom resolution (typically >80%) when RN resected, but recurrence of RN in adjoining brain is possible if underlying factors persist.
- **Hyperbaric oxygen:** Small series report 40–60% radiologic improvement with HBOT protocols (20–40 sessions); a systematic review suggests benefit but evidence is low-level. HBOT side effects (barotrauma) are minimal compared to steroids, making it an option if available.

Follow-up Protocols

Consensus guidelines (e.g. NCCN) advise frequent MRI surveillance after SRS, both to monitor control and catch RN early. NCCN recommends **MRI brain every 2–3 months for 1–2 years, then every 4–6 months indefinitely**. Because one-third of SRS-treated lesions transiently enlarge (“pseudoprogression”), stable follow-up imaging (often >2 sequential scans) may be needed to confidently diagnose RN. Any new lesion enlargement prompts the RN vs recurrence diagnostic workup as above. Neurocognitive and neurologic assessments should accompany imaging; RN is often suspected when new deficits correlate with imaging changes in the radiation field. In research protocols, advanced imaging may be repeated at 3–6 month intervals until RN stabilizes or resolves.

Discussion

Radiation necrosis remains a significant limitation of intracranial stereotactic radiotherapy. Its incidence has decreased in recent trials due to more stringent dose-volume constraints and use of fractionation for larger targets. However, with expanding indications (e.g. multiple mets, re-irradiation, combination immunotherapy), RN is a growing clinical issue. Risk mitigation requires careful planning: minimizing high-dose spill to normal brain (e.g. strict V12 limits) and considering fractionated schedules for lesions >1–2 cm. The IJROBP “HyTEC” review provides quantitative NTCP models to guide these limits.

Predictive models (nomograms) combining factors (V12, dose, tumor volume, systemic therapy) have been proposed but need prospective validation. The Cureus series (Nissen 2022) highlights concurrent systemic therapy and post-surgical adjuvant RT as risks; this underscores the complexity as many patients receive multimodal therapy. Modern immunotherapies may amplify RN risk by disrupting vascular repair; emerging data suggest immunotherapy/RN interactions that must be further studied.

Imaging remains imperfect. Multimodal protocols are advocated: when conventional MRI is equivocal, proceed to perfusion MRI and amino-acid PET. Most centers now use DSC perfusion routinely for enlarging post-SRS lesions. Amino-acid PET (if available) is often the most accurate noninvasive test. Despite these tools, tissue diagnosis is occasionally required, especially when treatments (e.g. immunotherapy continuation vs RN-directed therapy) hang in the balance.

Management is moving towards personalized algorithms. Our synthesis suggests:

- **Observation** is reasonable for small, asymptomatic RN in non-eloquent areas (studies show spontaneous stabilization in some cases).
- **Medical therapy** (steroids → bevacizumab) for symptomatic or progressive RN, often effective. The meta-analysis indicates bevacizumab should be considered early if steroids fail, given its high efficacy.
- **Neurosurgical intervention** for refractory cases or diagnostic need. LITT offers a less invasive surgical option; the meta-analysis suggests similar efficacy with fewer systemic effects than bevacizumab.
- **Preventive measures:** Strategies like prophylactic steroids are not clearly beneficial for RN (no studies support preemptive treatment). Some centers use short steroid courses post-SRS for large lesions, but data are anecdotal.

Open questions include optimal bevacizumab dosing/duration, long-term outcomes after LITT, and the role of new agents (e.g. anti-TNF α , statins) in RN. The rarity of RN as an endpoint has limited large trials, but meta-analyses like Gecici 2024 help clarify comparative effectiveness.

Conclusions and Recommendations

Radiation necrosis is an important SRS complication with variable incidence. Key recommendations:

1. **Prevention:** Limit V12/V10 volumes by planning and use fractionation for high-risk lesions. Consult published NTCP models (e.g. HyTEC) during planning.
2. **Monitoring:** Use a structured follow-up protocol (e.g. MRI q2–3 months for 2 years). Have low threshold to evaluate enlarging lesions with advanced imaging.
3. **Diagnosis:** Adopt a multimodal imaging approach: perform DSC perfusion MRI and consider amino-acid PET if available. If uncertainty persists and clinical decisions hinge on it, obtain tissue (biopsy or resection).
4. **First-line therapy:** Treat symptomatic RN with corticosteroids. Taper as quickly as possible. If steroids are required for >4–6 weeks or symptoms recur, escalate to anti-VEGF therapy.
5. **Bevacizumab:** Use 5–10 mg/kg IV q2–3 weeks for 4–6 cycles. Monitor for HTN/proteinuria. Expect clinical/radiologic improvement in most patients.
6. **Surgery/LITT:** Consider for lesions causing mass effect or refractory to medical therapy. LITT may be preferable for deep lesions or patients unfit for open surgery. Surgical pathology should guide further therapy.
7. **Adjuncts:** Bevacizumab can often facilitate steroid discontinuation. Emerging therapies (HBOT, novel drugs) should be considered experimental and tailored to individual cases.
8. **Reporting:** Future studies should standardize RN definitions, include volumetric dose data, and report symptomatic vs radiographic RN separately.

Ongoing research (e.g. trials of immunotherapy combinations, neuroprotectants) will further refine RN management. Multidisciplinary collaboration (radiation oncology, neurosurgery, neuro-oncology, neuroradiology) is essential for optimal RN care.

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