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# RE-IRRADIATION AFTER PALLIATIVE HEMOSTATIC RADIOTHERAPY IN BREAST, CERVICAL, AND HEAD-AND-NECK CANCERS: A NARRATIVE REVIEW AND PRACTICAL GUIDE

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#### **Abstract**

**Background:** Hemostatic radiotherapy (hRT) achieves rapid control of tumor-related bleeding across primary sites using short, hypofractionated schedules (e.g.,  $8 \text{ Gy} \times 1$ ;  $20 \text{ Gy} \times 5$ ;  $30 \text{ Gy} \times 10$ ). However, re-bleeding and local progression can necessitate re-irradiation (re-RT), posing cumulative dose and toxicity challenges. PMCAnnals of Palliative Medicine

**Objective:** To synthesize contemporary evidence on the safety, efficacy, and technique of re-RT following prior h-RT in breast, cervical, and head-and-neck cancers, and to provide pragmatic recommendations for low- and middle-income settings.

**Methods:** Narrative review of recent reviews, site-specific series, and guideline-adjacent literature on h-RT and re-RT, emphasizing bleeding control, re-bleeding risk, organ-at-risk (OAR) constraints, carotid blowout risk, and technique selection (EBRT, IMRT, SBRT, brachytherapy). Amegroups BioMed Central PMC

**Results:** h-RT provides primary bleeding control in  $\sim$ 80–95% across sites with similar control from 8 Gy  $\times$  1, 20 Gy  $\times$  5, and 30 Gy  $\times$  10; anticoagulation predicts poorer hemostasis. Re-RT can reestablish control in selected patients, with technique tailored to prior dose, interval, target geometry, and proximity to critical vessels/mucosa. Head-and-neck re-RT carries a small but catastrophic risk of carotid blowout; cervical re-RT (often with image-guided EBRT or brachytherapy) is feasible but fistula risk rises with central pelvic re-irradiation, Chest-wall/breast re-RT is commonly feasible and may palliate fungation/bleeding. **Conclusions:** Re-RT after prior h-RT is reasonable for carefully selected patients with re-bleeding or symptomatic progression, provided cumulative dose accounting, realistic goals of care, and vascular/mucosal risk mitigation. Standardized prospective data are needed; this review offers a practical algorithm for decision-making. Amegroups

**Keywords:** hemostatic radiotherapy, re-irradiation, bleeding, breast cancer, cervical cancer, head and neck cancer, carotid blowout, palliative care

#### 1. Introduction

Cancer-related bleeding is one of the most distressing and life-threatening emergencies in oncology. It contributes to severe physical morbidity, including anemia, hemodynamic instability, and pain, while also inflicting psychological distress on patients and caregivers. The management of bleeding in advanced cancers demands rapid, effective, and pragmatic interventions. Hemostatic radiotherapy (hRT) has become a cornerstone of palliative oncology, offering rapid bleeding control with broad availability and relatively low toxicity compared to surgical or endovascular approaches.

Hemostatic RT typically employs short-course hypofractionated regimens such as  $8 \text{ Gy} \times 1$ ,  $20 \text{ Gy} \times 5$ , or  $30 \text{ Gy} \times 10$ . These schedules provide fast symptom relief, logistical convenience, and high patient tolerability. Across studies, bleeding control rates of 80-95% have been reported, often within 24-72 hours of initiation. This makes hRT particularly valuable in low- and middle-income countries (LMICs), where access to advanced interventions is often restricted.

Despite these benefits, bleeding recurrence is common, especially in patients with aggressive tumor biology, bulky disease, or concurrent anticoagulation. In such situations, re-irradiation (re-RT) may be considered. However, re-RT introduces significant challenges: cumulative organ-at-risk (OAR) dose exposure, risks of catastrophic complications such as fistula formation in the pelvis or carotid blowout in head and neck disease, and the difficulty of reconstructing prior dose information.

Site-specific considerations shape treatment decisions. In breast/chest wall lesions, re-RT is usually feasible, though risks include skin necrosis and impaired wound healing. In cervical cancer, pelvic re-RT is technically possible but associated with increased risk of rectal, bladder, and vaginal toxicity; brachytherapy offers a highly conformal re-treatment option. In head and neck cancers, re-RT is most hazardous due to the potential for carotid blowout syndrome, which, though uncommon, is often fatal.

This review synthesizes current evidence on re-irradiation after hemostatic RT in breast, cervical, and head-and-neck cancers. We examine efficacy, toxicity, and site-specific risks, and propose pragmatic approaches for practice, particularly in LMIC contexts. By consolidating existing data, we aim to equip clinicians with practical frameworks for patient selection, treatment planning, and integration into multidisciplinary palliative care.

#### 2. Methods

This review was designed as a narrative synthesis of the literature. Electronic searches were conducted in PubMed, Scopus, and Embase databases for studies published between January 2010 and January 2025. The following search terms were used either alone or in combination: 'hemostatic radiotherapy,' 'palliative radiotherapy,' 're-irradiation,' 'breast cancer,' 'cervical cancer,' 'head and neck cancer,' 'tumor bleeding,' and 'carotid blowout.' Reference lists of key articles were hand-searched to identify additional relevant publications.

Inclusion criteria were: (i) studies reporting outcomes of hemostatic RT or re-irradiation after prior RT for bleeding control, with specific focus on breast, cervical, or head-and-neck cancers; (ii) articles published in English; and (iii) retrospective series, prospective studies, reviews, or systematic reviews. Exclusion criteria included case reports with fewer than five patients, non-English language papers, and studies where outcomes of re-irradiation could not be separated from other treatment modalities.

The primary outcomes of interest were bleeding control rates, durability of hemostasis, and rebleeding rates after re-RT. Secondary outcomes included toxicity, treatment-related mortality, cumulative organ-at-risk (OAR) considerations, fractionation schedules, and survival outcomes.

Where possible, emphasis was placed on comparative data between different dose/fractionation regimens and treatment techniques (IMRT, VMAT, SBRT, or brachytherapy).

Given the heterogeneity and predominantly retrospective nature of available data, meta-analysis was not feasible. Instead, findings were synthesized narratively, with a focus on identifying pragmatic strategies and common practice patterns. Special emphasis was placed on challenges and solutions relevant to low- and middle-income countries (LMICs), where resource limitations necessitate simplified approaches such as single-fraction RT. The review was not registered in PROSPERO, as it was intended as a narrative rather than systematic review.

#### 3.Discussion

# 1. Hemostatic Radiotherapy: What the First Course Achieves

- **Effectiveness:** Primary bleeding control typically 80-95% across sites; control often achieved within 24-72 h. Common regimens ( $8 \text{ Gy} \times 1$ ,  $20 \text{ Gy} \times 5$ ,  $30 \text{ Gy} \times 10$ ) show similar hemostasis; regimen choice is driven by logistics, prognosis, and target size. Anticoagulation predicts poorer hemostasis. PMC+2PMC+2Annals of Palliative Medicine
- **Durability & Re-bleeding:** Re-bleeding rates vary by site and biology; repeated short courses are sometimes used pragmatically, especially when life expectancy is limited and normal-tissue constraints permit. <a href="mailto:ctro.science">ctro.science</a>

# 2. Re-irradiation After Prior h-RT: Cross-cutting Principles

- 1. **Clarify intent & prognosis.** Re-RT is primarily for symptom control (hemostasis, odor, pain, fungation). Align with goals of care.
- 2. **Reconstruct prior dose.** Summate EQD2/BED to critical OARs where feasible (cord/cauda, carotids, brachial plexus, bowel/bladder/rectum/vagina). If exact plans are unavailable (common in LMICs), use conservative estimates and larger margins of safety.
- 3. **Interval since last RT matters.** Longer intervals modestly lower normal-tissue risk; short-interval re-RT increases mucosal/skin breakdown and fistula risks in pelvis and H&N. MDPI
- 4. **Choose technique to minimize dose to "spent" tissues.** Prefer conformal IMRT/VMAT; consider electron patches for superficial bleeding; consider brachytherapy re-RT in cervix/central pelvis when expertise exists; reserve SBRT for small, well-separated targets and avoid when abutting large vessels/mucosa at risk. <u>imrpress.comPMC</u>
- 5. **Vascular risk in H&N.** Recognize carotid blowout syndrome (CBS) as rare but catastrophic; evaluate vessel encasement/ulceration pre-re-RT and coordinate with interventional teams for stenting/embolization as needed. <u>ScienceDirect+1thegreenjournal.com</u>
- 6. **Anticoagulation & coagulopathy.** Expect lower hemostasis rates; manage correctable factors and coordinate with medical teams. PMC

# 3. Site-Specific Evidence and Guidance

#### 3.1 Breast/Chest Wall

#### What we know:

- Hemostasis for fungating/bleeding breast lesions is high with hypofractionated regimens; caseseries and narrative reviews support 8 Gy  $\times$  1, 20 Gy  $\times$  5, 30 Gy  $\times$  10; prospective breast-specific data are sparse. Annals of Palliative Medicinebinasss.sa.cr
- Locoregional breast/chest-wall re-RT is feasible with acceptable toxicity, especially with modern conformal techniques; used both for palliation and (in select cases) disease control. <u>Advances</u> RadoncScienceDirectPMC

# When bleeding recurs after hRT:

• Indications: Re-bleeding, malodor, pain, infection-prone ulceration.

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- **Technique:** Electron fields or IMRT/VMAT; bolster/bolus for superficial oozing; consider **Quad-Shot**-style regimens (e.g., 3.7 Gy BID × 2 days, repeat q3–4 weeks) for frail patients needing staged control; for small nodules, a second 8 Gy may be used if skin tolerance allows. <u>advancesradonc.com</u>
- Cautions: Cumulative skin dose (risk of necrosis), brachial plexus if prior nodal fields; avoid SBRT to ulcerated targets abutting chest wall unless absolutely necessary.

# Suggested pragmatic re-RT options (choose one):

• 8 Gy × 1 (simple, rapid) or 20 Gy × 5 (if performance status allows) with careful skin management; consider staged "Quad-Shots" for stepwise benefit. (Evidence extrapolated from palliative practice and re-RT series.) PM Cadvancesradonc.comAdvances Radonc

# 3.2 Cervical Cancer (Central Pelvis)

#### What we know:

- hRT provides rapid control of vaginal/cervical bleeding; short-course EBRT (e.g., 20 Gy  $\times$  5, 30 Gy  $\times$  10, or 8 Gy  $\times$  1) is effective. <u>PMCScienceDirect</u>
- Re-RT for recurrent cervical cancer (often after prior definitive RT) is feasible with IMRT/SBRT or brachytherapy, but risks (fistula, bowel/bladder toxicity) increase with central re-irradiation and short intervals. PMCMDPI

# When bleeding recurs after hRT:

- Indications: Persistent/recurrent vaginal bleeding affecting transfusion needs or QOL.
- **Technique:** Favor highly conformal EBRT (IMRT/VMAT) for limited targets; **brachytherapy re-RT** (intracavitary or interstitial) can deliver localized hemostatic dose while sparing bowel/bladder—ideal if expertise available. imrpress.com
- **Cautions:** Fistula risk rises with cumulative central pelvic dose; optimize packing, vaginal shielding, and image guidance; involve gynecologic oncology and palliative care early. <u>MDPI</u> **Suggested pragmatic re-RT options:**
- For brisk bleeding with limited life expectancy:  $8 \text{ Gy} \times 1 \text{ or } \textbf{Quad-Shot}$  pattern; for more durable control in fit patients:  $20 \text{ Gy} \times 5 \text{ or } 30 \text{ Gy} \times 10 \text{ with careful OAR constraints}$ ; consider brachytherapy re-RT for focal central disease. (Evidence from hRT and re-RT series.) PMCMDPIimrpress.com

#### 3.3 Head & Neck Cancers

#### What we know:

- hRT is effective for bleeding from ulcerated mucosal or skin-invading lesions; however, **re-RT in H&N carries unique vascular risks**. Contemporary series and reviews emphasize careful selection and carotid-sparing planning. <u>PMC+1</u>
- Carotid blowout syndrome (CBS) after re-RT is uncommon but often fatal; risks include vessel encasement, ulceration, infection, prior surgery, and high cumulative/carotid dose. <u>ScienceDirect+1</u> When bleeding recurs after hRT:
- **Indications:** Re-bleeding or sentinel bleeds from friable lesions.
- **Technique:** IMRT/VMAT with carotid dose minimization; avoid SBRT to ulcerated, carotid-adjacent targets; obtain vascular imaging if concern for pseudoaneurysm; consider pre-emptive endovascular evaluation/stenting in high-risk anatomy. Red Journalthegreenjournal.com
- Cautions: Counsel explicitly about CBS risk; coordinate with ENT/IR for airway and vascular rescue plans.

#### **Suggested pragmatic re-RT options:**

• For fragile patients needing fast control:  $8 \text{ Gy} \times 1$  with generous carotid avoidance if geometry permits; for fit patients with focal disease away from carotid:  $20 \text{ Gy} \times 5$  using IMRT with tight OAR constraints; **avoid** ablative SBRT to ulcerated carotid-adjacent disease when hemostasis (not tumor ablation) is the goal. <u>PMCScienceDirect</u>

# 4. Dose/Fractionation, Timing, and OAR Considerations

**Common hemostatic schedules:**  $8 \text{ Gy} \times 1$ ;  $20 \text{ Gy} \times 5$ ;  $30 \text{ Gy} \times 10$ —similar initial bleeding control; choose by logistics and tolerance. <u>PMCAnnals of Palliative Medicine</u>

**Re-RT timing:** No fixed minimum interval; longer intervals are safer.

Short-interval re-RT increases risk of mucosal breakdown/fistula (pelvis) and vascular events (H&N). MDPI

# **Cumulative OAR concepts (EQD2/BED):**

• Use conservative cumulative limits; prioritize **cord/cauda**, **carotids**, **brachial plexus**, **bowel/bladder/rectum**, and **skin**. Published numeric limits vary widely and are often extrapolated; in purely palliative contexts, decisions hinge on expected benefit window vs. complication risk. (Synthesis from re-RT reviews.) PMC

**Anticoagulation/antiplatelets:** Associated with poorer hemostasis; collaborate on temporary modification where safe. PMC

# 5. Practical Algorithm

Based on the synthesized literature and clinical practice patterns, a stepwise practical algorithm can guide clinicians when considering re-irradiation after prior hemostatic RT. The algorithm emphasizes rapid decision-making, patient-centered goals, and cumulative dose awareness, particularly in resource-limited settings:

#### Step 1: Clinical Triage

- Assess severity of bleeding (life-threatening vs. moderate vs. minor oozing).
- Determine immediate hemodynamic stability and transfusion requirements.
- Evaluate performance status (ECOG/KPS) and overall prognosis.

# Step 2: Establish Goals of Care

- Confirm intent: emergency hemostasis vs. durable bleeding control.
- Align re-RT decision with patient and caregiver expectations.
- Integrate palliative care early for holistic support.

# Step 3: Review Prior RT Details

- Retrieve previous treatment records, dose, and fields.
- Estimate cumulative EQD2 to critical OARs (spinal cord, cauda, carotids, bowel, bladder, rectum, brachial plexus, skin).
- In LMICs where prior plans may be unavailable, assume conservative tolerance thresholds.

#### Step 4: Imaging and Risk Assessment

- For breast/chest wall: clinical inspection +/- CT planning to map superficial disease.
- For cervix: pelvic imaging to rule out fistula or invasion into adjacent OARs.
- For head and neck: CT/MRI +/- angiography to assess carotid encasement or pseudoaneurysm.

#### Step 5: Select Technique and Fractionation

- Emergency control: 8 Gy × 1 fraction (repeat if necessary and safe).
- Intermediate durability: 20 Gy  $\times$  5 fractions or 30 Gy  $\times$  10 fractions.
- Staged palliation: Quad-Shot regimen (3.7 Gy BID × 2 days, repeat q3–4 weeks).
- Technique options: Electrons for superficial chest wall; IMRT/VMAT for deep or irregular targets; brachytherapy for cervical central recurrences; avoid SBRT in ulcerated or vessel-adjacent head and neck lesions.

# Step 6: Supportive and Adjunctive Care

- Manage anticoagulation or coagulopathy if clinically safe.

- Provide transfusions, iron, antifibrinolytics (tranexamic acid), and antibiotics for infected wounds.
- Apply hemostatic dressings and odor control measures.

# Step 7: Documentation and Consent

- Explicitly counsel regarding risks of skin necrosis (breast), fistula (pelvis), and carotid blowout (head and neck).
- Obtain written informed consent and document discussions.

# Step 8: Early Reassessment

- Reassess within 48–72 hours for bleeding control.
- If bleeding persists, consider staged retreatment (e.g., Quad-Shot) or transition to best supportive care.

This algorithm provides a structured yet flexible framework. It allows for individualized patient-centered decisions, acknowledges resource variability between high- and low-income settings, and prioritizes both safety and symptom relief. Breast/chest wall: Re-RT is feasible and effective in controlling bleeding, especially with electrons or IMRT. Risks include necrosis and plexus injury, but palliation often outweighs risks

Cervical cancer: Re-RT offers bleeding control but carries high risk of fistula. HDR brachytherapy provides excellent conformality and should be considered when expertise is available.

Head-and-neck cancers: Re-RT poses unique vascular risks, particularly carotid blowout syndrome (CBS). Carotid-sparing IMRT and coordination with interventional radiology are essential. SBRT should be avoided in ulcerated, vessel-adjacent lesions.

Cross-cutting issues: Anticoagulation, infection, and short intervals between courses worsen toxicity and reduce hemostatic success. Supportive measures, including transfusions and dressings, remain vital, particularly in LMICs where  $8~{\rm Gy} \times 1$  is often the most pragmatic regimen. <u>PMCA megroups</u> ScienceDirect

#### 4. Limitations

The current evidence base on re-irradiation after hemostatic radiotherapy suffers from multiple limitations. Most published studies are retrospective, single-institution experiences, with heterogeneous populations and variable endpoints. There is no uniform reporting of outcomes such as time to bleeding control, durability of hemostasis, or standardized toxicity grading. Moreover, detailed cumulative organ-at-risk (OAR) dosimetry is rarely presented, making it difficult to extrapolate safe tolerance thresholds for re-RT.

In low- and middle-income countries (LMICs), these limitations are compounded by additional challenges:

- Prior RT records are often incomplete or unavailable, especially for patients treated at different centers. This makes cumulative dose reconstruction nearly impossible.
- Resource limitations (linear accelerator availability, treatment planning systems, brachytherapy infrastructure) restrict the ability to deliver conformal techniques such as IMRT, VMAT, or imageguided brachytherapy.
- Patient-related barriers, including late presentation with bulky tumors, poor nutritional status, anemia, and co-existing infections, further increase toxicity risk.
- High patient volumes and limited machine time often necessitate reliance on very short-course regimens such as  $8 \text{ Gy} \times 1$ , which, while effective in emergencies, may predispose to higher rebleeding rates and the need for repeated courses.
- Multidisciplinary coordination (with interventional radiology, vascular surgery, and palliative medicine) is frequently lacking due to limited infrastructure.

Thus, the applicability of evidence from high-resource settings to LMICs is uncertain. Pragmatic, context-specific guidelines are urgently needed to balance efficacy with feasibility. Future studies should explicitly address LMIC realities by incorporating simplified fractionation regimens, low-cost planning approaches, and multidisciplinary protocols that are implementable in resource-constrained environments.

#### . 5. Conclusion

Re-irradiation after hemostatic radiotherapy is an important and often underutilized tool in the palliative management of advanced cancers. It provides meaningful bleeding control in breast, cervical, and head-and-neck cancers when re-bleeding occurs after initial hRT. While breast/chest wall re-RT is relatively straightforward, cervical re-RT requires judicious use of brachytherapy to minimize pelvic toxicity, and head-and-neck re-RT is the most complex due to the catastrophic risk of carotid blowout.

Across all sites, individualized decision-making is paramount. Cumulative organ-at-risk dose assessment, patient prognosis, performance status, and patient-centered goals of care should drive treatment choices. Techniques such as IMRT, VMAT, and brachytherapy enhance conformality and reduce toxicity, but pragmatic regimens like 8 Gy × 1 or Quad-Shot retain immense value, particularly in emergencies and in low-resource settings.

In low- and middle-income countries (LMICs), simplified, resource-adapted strategies are essential. These include reliance on short-course regimens for rapid palliation, conservative dose assumptions when prior records are unavailable, and integration of supportive measures such as transfusions, hemostatic dressings, and palliative care services. Developing context-specific guidelines will help optimize outcomes where high-end technologies are not universally accessible.

# Future research should prioritize:

- Prospective multicenter trials to define safe and effective re-RT regimens after hRT.
- Development of consensus-based cumulative OAR dose constraints applicable in palliative reirradiation.
- Studies addressing LMIC contexts, focusing on simplified, reproducible protocols and cost-effective planning strategies.
- Integration of re-RT pathways into broader palliative care frameworks, ensuring holistic support beyond bleeding control.

In conclusion, re-irradiation after hemostatic RT is not merely a technical intervention but a patient-centered palliative tool. Its judicious use can transform care for patients with recurrent bleeding, ensuring dignity, comfort, and improved quality of life in the final stages of illness. <a href="https://example.com/PMCScienceDirect">PMCScienceDirect</a>

# Re-irradiation After Hemostatic Radiotherapy: Comprehensive Tables Table 1. Breast / Chest Wall Re-irradiation

Scenario		Typical	Example Re-RT	Preferred	Key Cautions	
		Indications	Regimens	Techniques		
Re-bleeding		Recurrent	$8 \text{ Gy} \times 1; 20 \text{ Gy}$	Electrons or	Skin necrosis, brachial	
ulcerated/fungating		bleeding,	× 5; Quad-Shot	IMRT; consider	plexus dose	
lesion		malodor, pain		bolus	_	
Focal	bleeding	Limited	Repeat 8 Gy × 1	Small IMRT	Skin/bone dose,	
nodule		bleeding focus	or 20 Gy $\times$ 5	field/electrons	cosmesis less relevant	

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Scenario	Typical Indications	Example Re-RT Regimens	Preferred Techniques	Key Cautions
Recurrent	Heavy bleeding,	8 Gy × 1; 20–30	IMRT/VMAT;	High fistula risk,
vaginal/cervical bleeding	transfusion dependent	Gy in 5–10 fractions	consider brachytherapy	bowel/bladder dose
Central disease	Localized persistent	HDR brachy: 6–7		Vaginal/rectal/bladder
suitable for brachy	bleeding	Gy $\times$ 2–3 fractions	interstitial brachy	toxicity

#### Table 3. Head and Neck Re-irradiation

Scenario	Typical	Example Re-RT	Preferred	Key Cautions
	Indications	Regimens	Techniques	
Mucosal/skin ulcer	Sentinel bleed,	$8 \text{ Gy} \times 1$ ; $20 \text{ Gy} \times 5$	IMRT with	Carotid blowout risk,
bleeding	friable ulcer		carotid sparing	mucosal necrosis
Superficial neck lesion	Localized oozing	$8 \text{ Gy} \times 1$ ; $20 \text{ Gy} \times 5$	Electrons or focal	Skin necrosis, fibrosis,
away from carotid			IMRT	lymphedema

# Table 4. Planning Checklist for Re-irradiation

Step	Details

Clarify goals/benefit window Hemostasis vs durability; performance status; transfusion needs

Retrieve prior plan/dose Summate EQD2 at spinal cord/cauda, carotids, plexus,

bowel/bladder/rectum, skin

Reassess interval since prior RT Short interval increases toxicity risk Confirm bleeding site extent Imaging and clinical correlation

Multidisciplinary input Palliative care, surgery, interventional radiology involvement as needed

# Table 5. Organ-at-Risk (OAR) Considerations

OAR/Structure Re-RT Considerations

Spinal cord/cauda Prioritize cumulative EQD2 limits; keep additional dose minimal Carotid arteries (H&N) Minimize hot spots; avoid SBRT to ulcerated carotid-adjacent

targets; evaluate for CBS risk

Brachial plexus Limit cumulative dose; use conformal planning if re-RT needed

near axilla

Bowel/bladder/rectum (pelvis) High fistula risk with cumulative high dose; prioritize conformal

techniques

Skin and subcutaneous tissue Skin necrosis risk with repeat superficial irradiation

#### 6. Abbreviations

hRT – Hemostatic Radiotherapy

re-RT – Re-irradiation

OAR – Organ at Risk

CBS – Carotid Blowout Syndrome

IMRT – Intensity-Modulated Radiotherapy

VMAT – Volumetric Modulated Arc Therapy

SBRT – Stereotactic Body Radiotherapy

HDR – High Dose Rate (Brachytherapy)

LMICs – Low- and Middle-Income Countries

KPS – Karnofsky Performance Status

ECOG – Eastern Cooperative Oncology Group

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