

Stereotactic Body Radiation Therapy (SBRT) vs Stereotactic Ablative Radiation Therapy (SABR): Does Terminology Differentiate Treatment Intent in Metastatic Cancer?

Description

The authors review published prospective trials and protocols on stereotactic radiation therapies for metastatic disease to determine whether the terms SBRT and SABR are being used differentially based on intent of treatment, defined by primary study outcome, and propose a distinct definition of each.

Learning Objectives

Upon completing this activity, the readers should be able to:

- appreciate the importance of clear and consistent terminology to clarify treatment intent in metastatic disease, and
- adopt the use of the term stereotactic ablative radiation therapy (SABR) in the setting of metastatic disease for treatments with ablative intent and adopt stereotactic body radiation therapy (SBRT) for treatments with palliative intent.

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Target Audience

- Radiation Oncologists
- Related Oncology Professionals

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Stereotactic Body Radiation Therapy (SBRT) vs Stereotactic Ablative Radiation Therapy (SABR): Does Terminology Differentiate Treatment Intent in Metastatic Cancer?

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Stereotactic body radiation therapy (SBRT) or stereotactic ablative radiation therapy (SABR) has an evolving role in the treatment of primary and metastatic cancer. Loosely defined in the United States as radiation therapy that delivers high-dose radiation within a single or very few (generally ≤ 5) fractions, various terms have been used interchangeably to describe stereotactic radiation therapies with no clear-cut terminology documented.¹ The term SABR emerged in 2010 as it was thought to more accurately describe the dose intensity of the treatment vs SBRT, and it was proposed that the term be used instead of SBRT.² Several trials on stereotactic radiation therapies have since been developed and published, yet the discourse surrounding preferred terminology within the literature remains unclarified.

Previous work has shown that patients undergoing treatment for metastatic cancer often do not

have an accurate understanding of the intent of therapy, and that this misunderstanding may influence their decisions about further treatments.³⁻⁵ In the setting of metastatic disease, stereotactic therapies may be administered with intent to either ablate disease or provide palliation. Confusion results from the interchangeable use of the term SABR, which implies ablative intent, and SBRT, which is agnostic toward treatment intent. We anticipate that clarification of this terminology could help avoid confusion for patients and physicians, ultimately improving communication with patients undergoing treatment for metastatic disease. Herein, we review published prospective trials and protocols on stereotactic radiation therapies for metastatic disease to determine whether the terms SBRT and SABR are currently being used differentially based on intent of treatment, defined by primary study outcome, and propose a distinct definition of each.

Evidence Review

We conducted a narrative review of the literature to identify and summarize prospective trials and protocols that investigated the use of stereotactic radiation therapies for patients with metastatic disease. A PubMed query was conducted (search query outlined in **Supplementary Text 1** available with the online version of this article at www.appliedradiationoncology.com). Trials and protocols were included if: 1) they evaluated the use of radiation therapy directed toward visceral or bone metastases, 2) the intervention included stereotactic radiation therapy, 3) they assessed a primary outcome related to treatment response, disease control, or quality of life, 4) they used a prospective study design, and 5) they were published between January 1, 2010 and September 5, 2020. Studies were excluded if 1) they were phase 1 or pilot studies, 2) they represented a secondary analysis of a previously published trial, or 3) they included pediatric patients. A hand search of the gray literature included relevant professional organization websites as well as ClinicalTrials.gov.

We categorized the trials we identified based on terminology used (SBRT vs SABR), and whether they were single arm or randomized.

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We also categorized the primary endpoint in each study based on treatment intent, either as “tumor control” if related to local control, progression-free survival, or overall survival; or “palliation” if related to relief of symptoms. Inclusion and categorization of each study was determined by 2 reviewers (KL, NJM), and discrepancies were resolved by a third reviewer (EFG). Fisher’s exact test was used to assess the association between trial terminology and primary endpoint category.

Findings

Overall, 48 trials met eligibility criteria, of which 40% (n = 19) had published their results,⁶⁻²⁵ and 60% (n = 29) were ongoing. Published studies are listed in **Table 1** and **Table 2**. Eight trials (17%) primarily used the term SABR, 36 (75%) used the term SBRT, and 4 (8%) used a different term to describe the intervention. Nineteen trials (40%) were randomized. Overall, 75% (n = 36) and 25% (n = 12) of the trials assessed a primary outcome categorized as tumor control or palliation, respectively. Primary outcome did not differ based on intervention terminology ($P = 0.41$). We also assessed the use of terminology in published randomized trials only, speculating that these are usually the most influential publications. This subset includes 8 studies, of which 4 use the term SBRT, 3 use the term SABR, and 1 uses local consolidative therapy. Of note, within this cohort, all studies assessing palliative endpoints used the term SBRT, and 3 of 5 studies assessing tumor control used the term SABR.

Discussion

Recent evidence from randomized clinical trials has shifted the way in which we approach the treatment of patients with limited metastatic disease, expanding indications for the use of stereotactic radiation therapy

with curative intent.²⁶ An updated analysis of the phase 2 SABR-COMET (NCT01446744) trial reported a median 22-month increase in overall survival at 5 years with SABR in patients with controlled primary yet oligometastatic disease compared to standard of care.¹¹ Other randomized trials that have investigated the effect of stereotactic therapies on outcomes related to survival and disease progression include Gomez et al (NCT01725165),^{6,7} Iyengar et al (NCT02045446),⁹ and the ORIOLE trial (NCT02680587).¹² The trials published by Gomez et al and Iyengar et al are both phase 2 randomized trials that showed prolonged progression-free survival in patients with oligometastatic non-small-cell lung cancer who received SABR compared with maintenance therapy. The recently published ORIOLE trial showed lower rates of disease progression at 6 months in patients with oligometastatic prostate cancer who received SABR compared with observation. Collectively, these trials suggest that SABR/SBRT may effectively prolong progression-free and overall survival in patients with oligometastatic disease, typically defined as disease with limited metastases to 1 or 2 other regions of the body outside of the site of primary disease.²⁷

While stereotactic radiation therapy has a promising role in the curative treatment of patients with oligometastatic disease, it also has an emerging role in the palliation of symptoms caused by metastatic cancer. Prospective studies have shown that SBRT is feasible in the palliation of bone metastases and may reduce cost and the amount of time patients spend receiving treatment.^{28,29} A recent randomized trial conducted at The University of Texas MD Anderson Cancer Center (NCT02163226) found that the use of SBRT vs standard multifraction radiation therapy for the treatment of symptomatic bone metastases resulted in higher rates of pain response.²¹ An additional phase 2 randomized trial published by Sprave et al (NCT02358720) found a more

rapid and durable pain response with SBRT compared with multifraction conventional palliative radiation therapy (30 Gy in 10 fractions) for patients with spinal bone metastases.²⁰ Although further evidence is needed before the efficacy of SBRT for the palliative treatment of bone metastases is fully understood and recommended for use in routine practice, there are technical advantages to this modality, and its use in the palliative setting has been increasing.^{30,31}

Despite the proposal to switch from the term SBRT to SABR in 2010,² several trials still use the term SBRT. The results of our literature review demonstrate no correlation between terminology and treatment intent amongst all studies, but when including only the most influential publications (randomized trials), there seems to be a selective choice in terminology based on the endpoint. Given these findings, it may be reasonable to suggest that the term SABR should refer to a type of stereotactic therapy that is delivered with curative intent for patients with metastatic disease, and that it is not synonymous but rather falls under the more encompassing term SBRT in this setting. We recognize that for most clinicians, the terms SBRT and SABR are often considered interchangeable, despite prior calls to standardize terminology. The term SABR represents a newer name for an already existing treatment and is thought to more accurately describe the dose intensity in addition to its aesthetic benefits. Nonetheless, the interchangeable use of the terms in clinical practice, despite the preference for the term SABR when publishing randomized trials aimed at tumor control for metastatic disease, likely creates unnecessary confusion.

Conclusion

Evidence is evolving on the use of stereotactic radiation therapies for both palliative and ablative treatment in the metastatic disease arena. With

| Table 1. Published Trials Assessing the Use of Metastasis-Directed Stereotactic Radiation for Tumor-Control Endpoints | | | | | | | | | | |
|---|------|--|-------|--|--------------------------|-----------------------------|-----------------------------|-----------|------------------------------|-----------------------|
| STUDY NAME | YEAR | ELIGIBLE PATIENTS | PHASE | INTERVENTION ARM | CONTROL ARM | PRIMARY ENDPOINT | STATISTICALLY SIGNIFICANT?* | TERM USED | JOURNAL | PMID |
| Randomized | | | | | | | | | | |
| Gomez, et al NCT03410043 | 2016 | NSCLC with 1-3 metastases, response to systemic therapy | 2 | Local consolidative therapy (RT or resection) | Maintenance treatment | Progression-free survival | Yes | n/a | Lancet Oncol/J Clin Oncol | 27789196/ 31067138 |
| Ost, et al STOMP/ NCT01558427 | 2017 | Recurrent prostate cancer with 1-3 extracranial metastases | 2 | SBRT or surgery to metastases | Surveillance | ADT-free survival | Yes | SBRT | J Clin Oncol | 29240541 |
| Iyengar, et al NCT02045446 | 2018 | NSCLC with up to 5 metastases | 2 | SABR plus maintenance chemotherapy | Maintenance chemotherapy | Progression-free survival | Yes | SABR | JAMA Oncol | 28973074 |
| Palma, et al SABR-COMET/ NCT01446744 | 2019 | 1-5 metastatic lesions | 2 | SABR to metastases | Palliative RT | Overall survival | Yes | SABR | Lancet/ J Clin Oncol | 30982687/ 32484754 |
| Phillips, et al ORIOLE/ NCT02680587 | 2020 | Recurrent hormone-sensitive prostate cancer with 1-3 asymptomatic metastases | 2 | SABR to metastases | Observation | Progression at 6 months | Yes | SABR | JAMA Oncol | 32215577 |
| Single-Arm | | | | | | | | | | |
| Collen, et al | 2014 | Oligometastatic NSCLC with 1-5 sites | 2 | 10 fraction SBRT to all disease sites | None | Complete metabolic response | n/a | SBRT | Ann Oncol | 25114022 |
| Nuytens, et al NTR1788 | 2015 | Oligometastases to lung | 2 | 3 fraction or 1 fraction SBRT to lung metastases | None | Local control | n/a | SBRT | Int J Radiat Oncol Biol Phys | 25636758 |
| Scorsetti, et al | 2015 | Colorectal cancer with 1-3 liver metastases | 2 | 3 fraction SBRT | None | Local control | n/a | SBRT | J Cancer Res Clin Oncol | 25245052 |
| Trovo, et al CRO 2012-47 | 2018 | Oligometastatic breast cancer with 1-5 sites | 2 | SBRT or IMRT to metastases | None | Progression-free survival | n/a | SBRT | Radiother Oncol | 28943046 |
| Arrieta, et al NCT02805530 | 2019 | NSCLC with 1-5 metastases | 2 | Radical consolidative therapy | None | Overall survival | n/a | n/a | Lung Cancer | 30885354 |
| Petty, et al NCT01185639 | 2019 | NSCLC with 1-5 metastases, response to systemic therapy | 2 | Consolidative radiation therapy | None | Progression-free survival | n/a | n/a | Int J Radiat Oncol Biol Phys | 30003996 |
| Weiss, et al NCT01573702 | 2019 | NSCLC on EGFR TKI with 1-5 progressive sites | 2 | Stereotactic radiation | None | Progression-free survival | n/a | n/a | Cancer Treat Res Commun | 30852467 |
| Redmond, et al NCT01752036 | 2020 | Spinal metastases having undergone surgery | 2 | Postoperative 5 fraction SBRT | None | Local control | n/a | SBRT | Int J Radiat Oncol Biol Phys | 31628959 |
| <p>Table of published randomized clinical trials assessing the use of stereotactic radiation therapy for metastatic disease with endpoints assessing tumor control. Trials are organized by randomized vs single-arm studies. *Statistical significance refers to whether a difference was demonstrated between intervention and control arms with regard to the primary endpoint.</p> <p>Key: NSCLC = non-small-cell lung cancer, RT = radiation therapy, SBRT = stereotactic body radiation therapy, ADT = androgen deprivation therapy, SABR = stereotactic ablative radiation therapy, IMRT = intensity-modulated radiation therapy</p> | | | | | | | | | | |

Table 2. Published Trials Assessing the Use of Metastasis-Directed Stereotactic Radiation for Palliative Endpoints

| STUDY NAME | YEAR | ELIGIBLE PATIENTS | PHASE | INTERVENTION ARM | CONTROL ARM | PRIMARY ENDPOINT | STATISTICALLY SIGNIFICANT?* | TERM USED | JOURNAL | PMID |
|--|------|-------------------------------|-------|--|-----------------------------|--|-----------------------------|-----------|------------------------------|----------|
| Randomized | | | | | | | | | | |
| Sprave, et al NCT02358720 | 2018 | Painful spinal metastases | 2 | Single-fraction SBRT | 10-fraction conventional RT | Pain response | No | SBRT | Radiother Oncol | 29843899 |
| Nguyen, et al NCT02163226 | 2019 | Painful bone metastases | 2 | Single-fraction SBRT | 10-fraction conventional RT | Pain response | Yes [†] | SBRT | JAMA Oncol | 31021390 |
| Pielkenrood, et al VERTICAL/ NCT02364115 | 2021 | Painful bone metastases | 2 | Standard SBRT | Standard conventional RT | Pain response | No | SBRT | Int J Radiat Oncol Biol Phys | 33333200 |
| Single-Arm | | | | | | | | | | |
| Wang, et al NCT00508443 | 2012 | Stable spinal metastases | 1-2 | 3-fraction SBRT | None | Frequency and duration of complete pain relief | n/a | SBRT | Lancet Oncol | 22285199 |
| Guckenberger, et al NCT01594892 | 2018 | 1-2 painful spinal metastases | 2 | 5- or 10-fraction SBRT | None | Pain response | n/a | SBRT | Cancer | 29499073 |
| Wardak, et al NCT00855803 | 2019 | Painful spinal metastases | 2 | Single-fraction SABR plus vertebroplasty | None | Pain response | n/a | SABR | Int J Radiat Oncol Biol Phys | 30684664 |

Table of published randomized clinical trials assessing the use of stereotactic radiation therapy for metastatic disease with endpoints assessing palliation. Trials are organized by randomized vs single-arm studies. *Statistical significance refers to whether a difference was demonstrated between intervention and control arms with regard to the primary endpoint.

[†]Study was powered to show noninferiority but did not note a significant difference between arms in terms of pain response. Key: SBRT = stereotactic body radiation therapy, RT = radiation therapy, SABR = stereotactic ablative radiation therapy

this split in the paradigm, there is an important opportunity to improve clarity surrounding treatment intent by using consistent terminology. Based on our review of published randomized control trials and protocols, the term SABR is more commonly used in the literature for oligometastatic disease in which stereotactic radiation therapy is administered with curative intent. In contrast, the term SBRT is more widely used and encompasses radiation therapy delivered with both palliative and curative intent to patients with incurable metastatic disease and oligometastatic disease, respectively. Therefore, we propose that a distinction be made and that the term SABR should be used in reference to stereotactic therapies delivered with curative intent for patients with oligometastatic disease, while the term SBRT should be used to describe radiation therapy

delivered with palliative intent to sites of metastases regardless of overall disease burden. We believe this distinction will reduce confusion in routine practice and ensure consistency in the publication of research on a single technique used for two distinct purposes.

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Supplementary Text 1:

SEARCH STRATEGY:

((("Neoplasm Metastasis"[MeSH] OR "metastases" OR "metastasis" OR "oligometastases" or "oligometastatic") AND ("Radiotherapy"[Mesh] OR "Radiation"[Mesh] OR "Radiotherapy, Conformal"[Mesh] OR "Radiosurgery"[Mesh] OR "Radiotherapy, Intensity-Modulated"[Mesh] OR "radiotherapy" OR "radiation") AND ("stereotactic body" OR "stereotactic" OR "stereotactic ablative" OR "ablative" OR "ablation" OR "SBRT" OR "SABR" OR "consolidative"))

Filter: Randomized trial, 1/1/2010-9/5/2020, English