

The abscopal effect: systematic review in patients with brain and spine metastases

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Abstract

Background. The abscopal effect is a rare phenomenon whereby local radiation induces a proposed immune-mediated anti-tumor effect at distant sites. Given the growing use of immunotherapies and systemic immune checkpoint inhibitors in neuro-oncologic practice, we aimed to review prior studies pertaining to this phenomenon in the context of tumor shrinkage both within the central nervous system as well as distant disease sites.

Methods. A systematic review in accordance with the PRISMA guidelines was conducted to identify all studies which assessed the abscopal effect in patients with treated metastatic cancer to the brain and/or spine. Articles were included if they reported the abscopal effect in patients (case studies) or if the abscopal effect was explicitly analyzed in case series with cohorts of patients with metastatic brain or spine tumors. Laboratory investigations and clinical trials investigating new therapies were excluded.

Results. Twenty reports met inclusion criteria [16 case reports, 4 case series ($n = 160$), total $n = 174$]. Case reports of the abscopal effect were in relation to the following cancers: melanoma (6 patients), breast cancer (3), lung adenocarcinoma (2), non-small-cell lung cancer (2), hepatocellular carcinoma (1), and renal cell carcinoma (1). Eleven patients had irradiation to the brain and 2 to the spine. Patients undergoing whole brain radiotherapy (6) had an average dose of 33.6 Gy over 8–15 fractions, and those undergoing stereotactic radiosurgery (5) had an average dose of 21.5 Gy over 1–5 fractions. One patient had radiation to the body and an intracranial abscopal effect was observed. Most common sites of extracranial tumor reduction were lung and lymph nodes. Ten case studies (57%) showed complete resolution of extra-CNS tumor burden. Median progression-free survival was 13 months following radiation. Four papers investigated incidence of abscopal effects in patients with metastatic melanoma to the brain who received immune checkpoint inhibitor therapy ($n = 160$); two papers found an abscopal effect in 35% and 52% of patients ($n = 16, 21$ respectively), and two papers found no evidence of abscopal effects ($n = 61, 62$).

Conclusions. Abscopal effects can occur following radiotherapy in patients with brain or spine metastases and is thought to be a result of increased anti-tumor immunity. The potential for immune checkpoint inhibitor therapy to be used in combination with radiotherapy to induce an abscopal effect is an area of active investigation.

Keywords

abscopal effect | brain metastasis | local radiation with distant anti-tumor effect | neuro-oncology | spine metastasis

The abscopal effect is an oncologic phenomenon in which radiation to one tumor site causes tumor regression in a distant, nonirradiated location. This effect was first described in the 1950s and has since been reported in numerous case studies.¹⁻³ While not completely understood, the abscopal effect is likely an immune-mediated mechanism where the tumor microenvironment is disrupted by local radiation, allowing improved antigen presentation with subsequent anti-tumor activity at distant sites.⁴

This phenomenon is of particular importance to the neurosurgical and neuro-oncology community as there have been multiple reports of the abscopal effect occurring following radiation treatment for metastatic disease to the brain.⁴⁻⁶ This is especially pertinent with the growing literature and use of immune checkpoint inhibitors (ICI), including anti-CTLA-4, Programmed-Death 1 (PD-1) and Programmed-Death Ligand 1 (PD-L1) antibodies in pre-clinical models and early clinical trials of primary and metastatic brain tumors, and the proposed immune-mediated synergistic effect of radiation and checkpoint inhibitor therapy.⁷⁻⁹ Importantly, understanding the characteristics of patients who might benefit from the abscopal effect and the potential to harness this effect as a therapeutic tool remain largely unknown.

To better communicate this phenomenon as it pertains to neurological surgeons and neuro-oncologists, we systematically reviewed the literature for instances of the abscopal effect in patients with metastatic disease to the brain or spine. We discuss the hypothesized mechanism underlying this phenomenon and directions for future investigation.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines¹⁰ were used to query the MEDLINE and PubMed databases for articles published between January 1, 1990 and September 1, 2021 using the following search criteria: ((abscopal effect OR bystander effect) AND ((brain OR spine OR metastases OR glioma OR glioblastoma)). For clarity in study methodology, the PICOS (Participants, Interventions, Comparators, Outcomes, Study Design) framework was followed: Participants were patients with metastatic primary cancer to the brain and or spine who experienced the abscopal effect. The intervention studied was radiotherapy for metastatic tumors. There were no direct comparators for this study; primary outcomes measured were location of abscopal effect and survival. Finally, both case studies and case reports were included (study design).

Inclusion and Exclusion Criteria

Studies were included if they: were published in English, reported clinical results, studied or showed evidence of abscopal effects, included patients with primary or metastatic central nervous system tumors, listed the neurosurgical pathology as the site of radiation or as the distant site, and reported outcomes data (progression-free survival, overall survival, or follow-up time). Case series

were included if they explicitly investigated the presence or absence of the abscopal effect and any subset of patients studied had metastases to the brain or spine. Studies investigating abscopal effects and reporting negative results were also included. It is important to note that studies describing the abscopal effect in patients on systemic therapy (particularly ICI) may blunt an understanding of the abscopal effect “on its own”; however, given the proposed synergistic mechanism between ICI and radiation induced immune responses, and the potential for these therapies to be utilized in tandem, these studies were included.

Studies were excluded if they were: review articles, laboratory investigations, or did not involve neurosurgical pathology (eg, irradiating liver metastases reduced the size of lymph node metastases). Clinical trials investigating novel therapeutics for brain tumors were also excluded.

Two independent reviewers screened titles and abstracts for relevance (DJP, BY). Following full-text review, a third author (TC) arbitrated the two lists to finalize the 18 studies included in analysis (Figure 1).

Data Collection and Analysis

Data was collected on patient presentation, radiation treatment details (dosage, fractions), and outcomes [time to abscopal effects, overall survival (OS), progression-free survival (PFS)]. Data from case reports were aggregated and averaged to determine radiation dosage, OS, PFS. Articles which did not report these findings were not included in calculations.

Results

A total of 1230 articles were queried. Of these, 55 studies remained following screening based on title and abstract for relevance. Of the 55 studies which underwent full-text analysis, 35 were excluded for the following reasons: did not contain evidence of primary or metastatic brain or spine tumor ($n = 15$), were review articles without unique patient reports ($n = 7$), referenced the abscopal effect but did not discuss it in a clinical context ($n = 3$), clinical trials of novel systemic therapies ($n = 2$), were not in English (1), and described in a pre-clinical animal model ($n = 2$). One article discussed an abscopal-like effect in a patient with glioblastoma but who did not have a secondary tumor; this study was excluded from the main analysis. Following exclusion of these studies, there were a total of 20 articles that met inclusion criteria, of which 16 were case reports, and 4 were retrospective case series.^{6,11-27} All studies were published between 2013 and 2021, with one article published in 1998.

A summary of the 16 case reports comprising 16 patients is shown in Table 1. Data were pooled and averaged to determine radiation dose and outcomes. There were 11 case reports of radiation to intracranial metastases resulting in extracranial abscopal effects (IC-EC).^{6,15-17,24-29} There were two reports of radiation to the vertebral column leading to extracranial responses (V-EC).^{13,14} There was one report of radiation to extracranial sites resulting in intracranial abscopal effect (EC-IC).¹¹ There were two reports of

soft tissue radiation leading to reduction in spine metastases.^{12,23} All included case reports are further described in Table 1.

The two most common cancers associated with abscopal effects were metastatic melanoma ($n = 6$) and breast cancer ($n = 3$). Of the 16 patients described in these case reports, 10 were on systemic therapy, including 6 on immune checkpoint inhibitors (PD-1/PD-L1 inhibitors: $n=4$, CTLA-4 inhibitors: $n = 1$). Of the patients who received systemic checkpoint inhibitor therapy, two patients had disease progression following ICI and prior to radiation, one patient had stabilization of tumor size following ICI and prior to radiation, and three patients received ICI concurrently with radiation. Other systemic chemotherapies included IL-2 ($n = 2$), BRAF inhibitor ($n = 1$), and EGFR tyrosine kinase inhibitor ($n = 1$); there were no overarching similarities in the group which received systemic therapy but not ICI (3 melanoma patients, 1 breast cancer patient, OS = 19 months) (Table 1). Five patients in the IC-EC cohort had whole brain radiotherapy (WBRT) with an average dose of 33.6 Gy (range 30–48, range: 8–15 fractions). Four patients underwent stereotactic radiosurgery for brain metastases (average dose of 21.5 Gy, range 20–25 Gy, 1–5 fractions).

The average time between the delivery of radiation and the discovery of the abscopal effect (on repeat scan) was 5.7 months; one report demonstrated an abscopal effect in an admitted patient in under 1 week.¹⁷ The most common locations for distant tumor reduction were lung ($n = 9$) and lymph nodes ($n = 5$). Sixty-three percent (10/16) of studies reported a complete or near-complete metabolic response and absence of all distant tumor foci following abscopal effect. The median progression-free survival was 14 months (2 case reports had PFS of 7, 10 years). Only two studies reported progression of disease subsequent to abscopal effect.^{13,17}

In one case report, a patient with metastatic lung cancer experienced an abscopal effect that occurred a second time following treatment for tumor recurrence.¹⁷ Following irradiation to the brain and subsequent abscopal effect, this patient saw progression of disease, and following irradiation to the thoracic spine, experienced a second abscopal effect. There was additionally one reported case of intracranial resolution following extracranial metastasis in a patient with metastatic lung cancer who received radiation to the axillary lymph nodes.¹¹

There were four case series explicitly investigating the abscopal effect in cohorts of patients with brain or spine metastases from metastatic melanoma ($n = 160$) (Table 2). In one study, 21 patients were included, of which 11 had a partial or whole abscopal response.²² Of those 11 with an abscopal response, 7 had an abscopal response following WBRT and one patient following vertebral irradiation (Table 2). In another study, of 16 patients with metastatic melanoma to the brain who underwent radiotherapy for brain metastasis while on ipilimumab therapy, 35% of noncranial lesions showed a decrease in lesion size. The authors found a 2.8-fold increased likelihood that the rate of extracranial lesion response improved following intracranial irradiation, however this did not achieve significance.²¹ In two case series comprising 68 patients with metastatic melanoma who received ICI and radiotherapy (36, 32 patients respectively), no evidence of abscopal effects were found (total $n = 61, 62$).^{19,20}

Discussion

Mechanisms and Clinical Characteristics of Patients with Abscopal Effect

First documented in 1958, the abscopal effect is derived from the Latin *ab* meaning “position away from” and *scopus* meaning “mark” or “target” and describes unexpected regression in metastatic lesions outside an irradiated field.¹ Since its initial description, it has been reported anecdotally but systematic research and observation was sparse due to its rare nature.² Potential mechanisms underlying the abscopal effect remain poorly understood, however, it is thought that radiotherapy may alter the tumor microenvironment and transient breakdown of the blood–brain barrier, leading to improved antigen presentation with a subsequent anti-tumor immune response at distant sites. One proposed mechanism is increased expression of calreticulin following radiation on the tumor cell surface, promoting phagocytosis by dendritic cells.^{2,5,30} Subsequently, dendritic cells then serve as antigen presenting cells, activating T-cells and inducing an anti-tumor response (Figure 2). Similarly, checkpoint inhibitors, such as PD-1/PD-L1 inhibitors or CTLA-4 inhibitors utilize the interaction between dendritic cells as antigen presenting cells and T-cell activation to induce an immune response against tumors.³¹ Accordingly, it is possible that the combination of radiotherapy and checkpoint inhibitors could have synergistic effect, which has been shown in pre-clinical models.⁷

We identified 16 individual case reports in which the abscopal effect was documented, of which 11 patients had radiotherapy to the brain, 2 had radiotherapy to the spine, and 3 had radiotherapy to other sites. Six patients included in the review were on immune checkpoint therapy, one patient with adenocarcinoma of the lung, one patient with unspecified NSCLC, and one patient with melanoma. Interestingly, six patients were not on any systemic therapy when the abscopal effect was noted. In these cases, radiation was generally performed for palliative measures, and patients presented back to the hospital for other causes (e.g. pneumonia) with subsequent staging imaging showing resolution of distant metastases. When discussing the abscopal effect for brain tumors, it appears that both SRS and WBRT are able to induce an abscopal effect for extracranial metastases.^{32,33} These findings are consistent with the results of other systematic reviews on the abscopal effect; Macki et al.³⁴ demonstrated that the abscopal effect for spine metastases was most common in patients with high doses of radiotherapy and on immunomodulatory therapy. Other reviews across multiple primary cancer subtypes and multiple metastatic locations have demonstrated the abscopal effect in similar populations and across similar cancers as our study, and similar to Macki et al.^{35,36} postulated that higher dosages may have an increased abscopal effect.

The incidence of the abscopal effect is still debated. While the predominance of case reports suggests it is a rare phenomenon, two retrospective studies of patients with malignant melanoma found when checkpoint inhibitors and

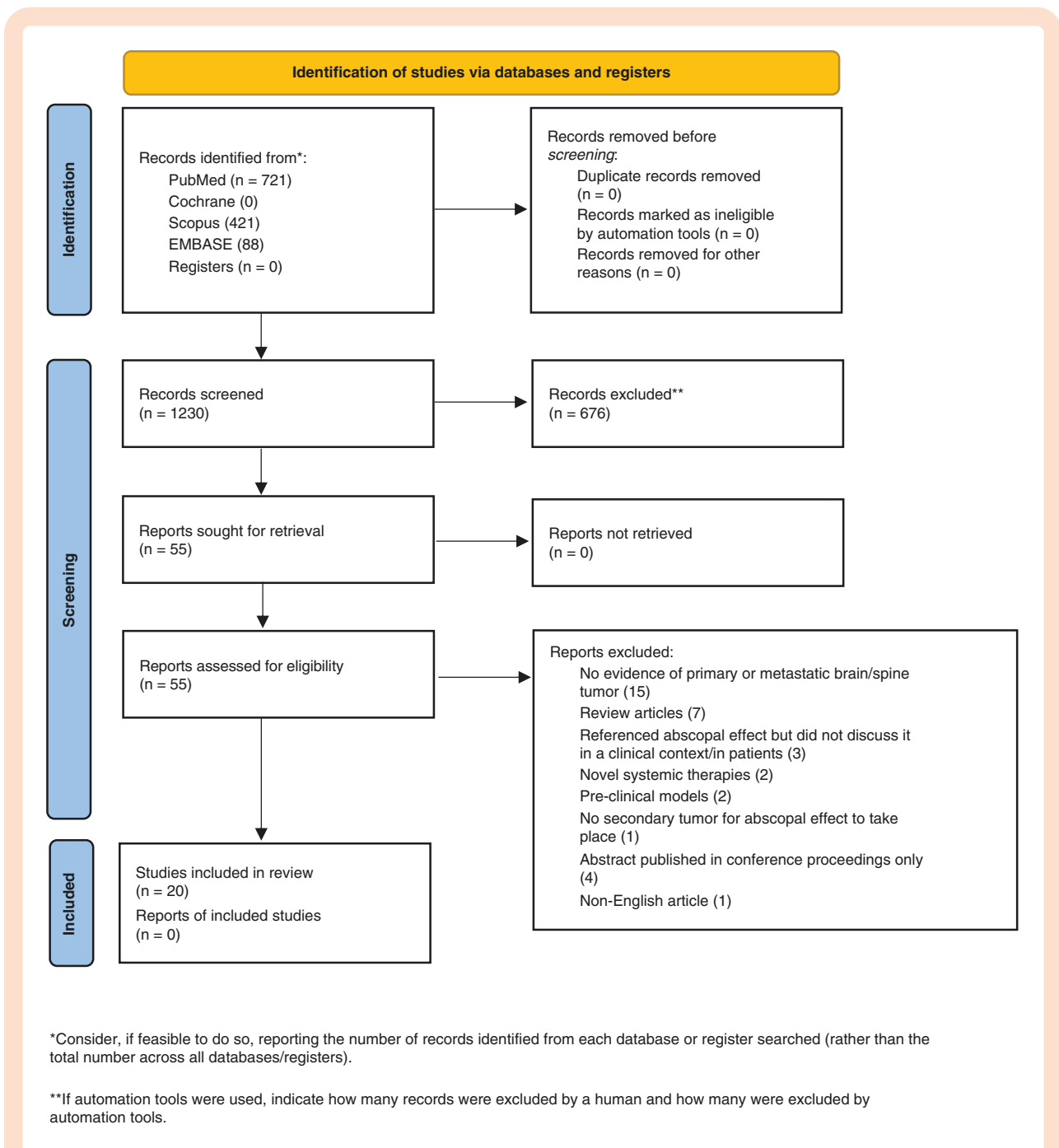


Figure 1 PRISMA flowchart demonstrating exclusion of studies from initial search query.

radiotherapy were combined, an abscopal effect was achieved in a significant proportion of patients 35% and 52% of patients, respectively.^{21,22} This is contradicted, however by two studies which found no evidence of the abscopal effect; conclusions from one of these studies, however, is limited as reduction in tumor size was primarily studied for CNS metastases which may be a significantly rarer phenomenon.²⁰ In addition, in one case report a patient experienced an initial abscopal effect (following irradiation of brain metastases) and subsequent progression of extracranial disease, with a second abscopal effect observed following irradiation

of a spinal metastasis.¹⁷ This suggests that there are systematic changes occurring which promote anti-tumor immunity and may be harnessed in future treatments. Factors influencing the development of abscopal effects may include timing of radiotherapy and immunotherapy, fractionated vs unfractionated therapy, or genetic subtypes which may be more immune-responsive. One of these factors that is noteworthy is the effect of varying fractionation regimens on the incidence of observed abscopal effect. One study suggests that varying fractionation dosage rather than single dose radiotherapy has been seen to induce an abscopal effect

Table 1 Summary of all case reports of abscopal effect in patients with metastatic brain or spine tumors

Study	Primary cancer	Sex (age)	Location of intracranial/spine metastases	Location of extracranial/extravertebral metastases	Systemic therapy	Radiation location (dose, fractions)	Abscopal effect location	Complete metabolic response? (Time)*	Progression-free survival (overall survival) (months)
Piercey et al. ¹¹	Melanoma ^a	M (67)	Parietal lobe Globus pallidus	LN	Anti-CTLA-4, Anti-PD-1, Anti-RANKL	Axilla (30, 10)	Lymph Nodes, Bone, Brain	Yes (2)	15 (N/R)
Sperduto et al. ²⁵	Melanoma ^b	F (36)	Caudate Parietooccipital L Frontal L	LN, soft tissues	cisplatin, interferon, vinblastine, IL-2	SRS (20/20/24, N/R)	Soft Tissue	Yes (NR)	132 (N/A)
D'andrea et al. ²⁷	Melanoma ^b	F (42)	BL hemispheres Thalamus	Chest Wall	BRAF inhibitor, MEK Inhibitor	WBRT (66, 33)	Chest wall	No (< 1)	2 (7)
Okwan-Duodu et al. ¹⁸	Melanoma ^b	F (50)	Pons Frontal L	Groin, LN	IL-2	WBRT (N/R, N/R)	Lung, Groin	Yes (6)	36 (N/A)
Igarashi et al. ²⁸	Oral Mucosal Melanoma ^b	M (74)	BL Frontal L Occipital	Spleen, liver	Anti-PD-1	WBRT (30,10)	Spleen, liver	Yes (2)	12 (N/A)
Stamell et al. ²⁹	Melanoma ^b	M (67)	Intracranial*	LN	Anti-CTLA-4	SRS (N/R, N/R)	Cutaneous	Yes (NR)	84
Leung et al. ²³	Breast ^c	F (65)	Spine (T8)	LN	None	Breast (50, 25)	Spine, Lymph Nodes	No (24)	48 (48)
Kim et al. ¹²	Breast ^c	F (37)	Spine (T)	Lung, Bone LN	None	Chest Wall (22.5, 5)	Lung, chest wall	No (1)	3 (14)
Azami et al. ¹³	Breast ^c	F (64)	Spine (Lumbar, Sacrum)	Breast, Lung, LN, bone	Aromatase Inhibitor	Lumbar spine (39, 20)	R breast, Lung, LN, bone (Femur), Lumbar Spine, Sacrum	Yes (10)	3 (21)
Chuang et al. ⁶	Adenocarcinoma ^b	F (74)	Brain (U/S)	N/A	None	WBRT (30, 10)	Lung	No (2)	2 (LTFU)
Hotta et al. ¹⁷	Adenocarcinoma ^b	F (42)	Brain (U/S) Spine (T)	N/A	Anti-PD-L1, EGFR TKI	WBRT (30, 10)	Lung	No (< 1)	5 (6)
Lin et al. ²⁶	Adenocarcinoma ^b	M (71)	Parietal L	N/A	Anti-PD-L1	WBRT (48, 8)	Lung	No (6)	16 (N/A)
Parisi et al. ²⁴	NSCLC ^b	F (79)	Brain (U/S)	Lung, Bone	Anti-PD-1	SRS (20, 1)	Lung, bone	Yes	16 (N/A)
Hamilton et al. ¹⁵	NSCLC ^b	M (47)	Frontal L	Left lung, left mediastinum	None	SRS (25, 5)	Chest wall, lung	Yes	7 (7)

*Time to progression

Table 1 Continued

Study	Primary cancer	Sex (age)	Location of intracranial/spine metastases	Location of extracranial/extravertebral metastases	Systemic therapy	Radiation location (dose, fractions)	Abscopal effect location	Complete metabolic response? (Time)*	Progression-free survival (overall survival) (months)
Ishiyama et al. ¹⁶	RCC ^b	F (68)	Spine (T8, 10) Temporal L	Adrenal, lung, mediastinum, bone	None	SRS (18, N/R)	Lung, LN	No	36 (36)
Ohba et al. ¹⁴	HCC ^c	M (76)	Spine (T2)	Liver	None	Thoracic spine (36, N/R)	Spine, liver	No	24 (N/A)

N/R, data point not reported; N/A, overall survival times that were assumed to persist through the publication date of the study as their mortality status was not explicitly stated; LN, lymph node; SRS, stereotactic radiosurgery; WBRT, whole brain radiotherapy; LTFU, lost to follow-up; NSCLC, non-small cell lung cancer; U/S, unspecified location; L, lobe; T, thoracic.

a = EC-IC, b = IC-EC, c = V-EC.

*Time to abscopal effect (months).

Table 2 Retrospective case series of patients with metastatic melanoma on immune checkpoint inhibitors, receiving radiotherapy

Study	Design	Cohorts	Pathology	Checkpoint inhibitors	Summary/abscopal effects and outcomes
Galli et al. ¹⁹	Retrospective series (61)	ICI + RT (36) Control (25)	Malignant melanoma with brain metastases	Anti-CTLA4 (23) Anti-PD1 (13)	No abscopal effects seen
Le Rhun et al. ²⁰	Retrospective series (62)	ICI alone (10) Non-ICI + SRS (20) ICI + SRS (32)	Malignant melanoma with brain metastases	Anti-CTLA4 Anti-PD1 Anti-PDL1 (Values N/R)	No abscopal effects seen
Schoenfeld et al. ²¹	Retrospective series (16)	ICI + SRS (16)	Malignant melanoma with brain metastases	Anti-CTLA4 (16)	11 of 31 extracranial lesions (35%) decreased in size 2.8x increase likelihood of extracranial index lesion response (NS, $P = .07$) Timing of ICI within three months of SRS enhances abscopal effect (63% vs 7%, $P = .003$)
Grimaldi et al. ²²	Retrospective series (21)	ICI + WBRT (9) ICI + SRS (4) ICI + Vertebral Radiation (2) ICI + Other SBRT (6)	Malignant melanoma with brain metastases	Anti-CTLA4 (21)	11 patients with abscopal response (52%) 7/11 patients with abscopal effect had local radiation to brain 40 mean days from RT to abscopal effect Median survival 22.4 months (AE) compared to 8.3 months (No AE)

ICI, immune checkpoint inhibitor; RT, radiotherapy; SRS, stereotactic radiosurgery; WBRT, whole brain radiotherapy; SBRT, stereotactic body radiotherapy.

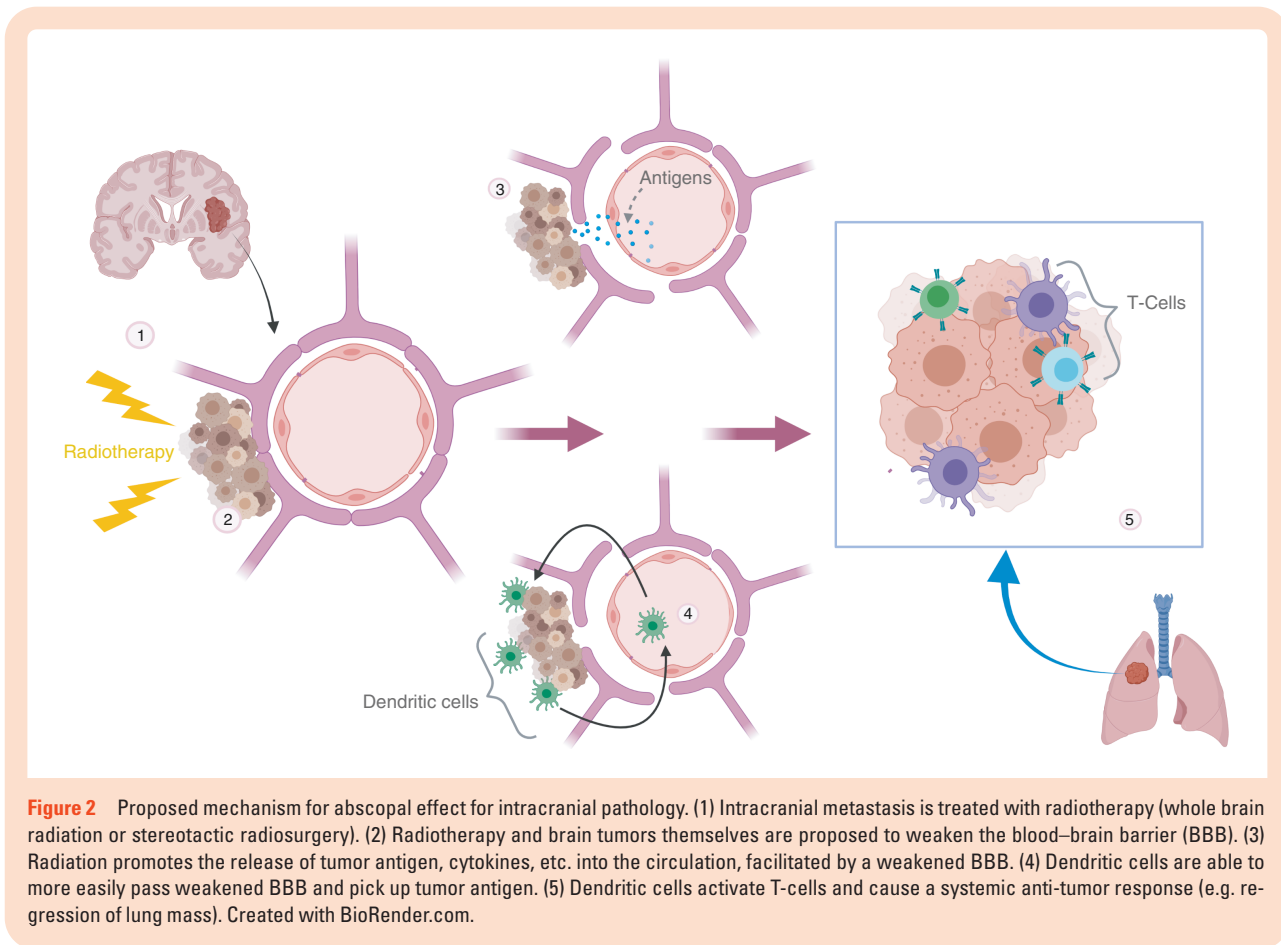


Figure 2 Proposed mechanism for abscopal effect for intracranial pathology. (1) Intracranial metastasis is treated with radiotherapy (whole brain radiation or stereotactic radiosurgery). (2) Radiotherapy and brain tumors themselves are proposed to weaken the blood–brain barrier (BBB). (3) Radiation promotes the release of tumor antigen, cytokines, etc. into the circulation, facilitated by a weakened BBB. (4) Dendritic cells are able to more easily pass weakened BBB and pick up tumor antigen. (5) Dendritic cells activate T-cells and cause a systemic anti-tumor response (e.g. regression of lung mass). Created with BioRender.com.

when in combination with anti-CTLA-4 antibodies in pre-clinical models. Within the study, mouse trials suggested that not only is their therapeutic potential for the incidence of abscopal effect when combining fractionated radiotherapy with immunotherapy treatment but that there also exists a specific therapeutic window in regard to optimal fractionation that can best induce a measurable abscopal effect and tumor specific T-cell mediated response.³⁷

Other systematic reviews have also demonstrated wide discrepancies in the prevalence of the abscopal effect—from under 10% to over 60% in individual studies.³⁸ This discrepancy is likely multifold: primarily, there are no clear consensus guidelines for the investigation or reporting of the abscopal effect. Accordingly, limited data could be reliably pulled from all manuscripts, including information regarding treatment timeline, radiotherapy details, follow-up details, surveillance protocols, or thresholds for declaring a tumor response “abscopal effect” (eg, percentage reduction). This represents an area of potential quality improvement in research, and standardized metrics for reporting would assist in supporting or dismissing claims regarding the incidence abscopal effect.

The Role of the Blood–Brain Barrier in the Abscopal Effect

Previously, the blood–brain barrier (BBB) was thought to create immune privilege within the brain, which was

supported by the general lack of therapeutics which could cross the BBB and take effect in the brain.^{39,40} However, growing evidence suggests immune responses can still occur, particularly when the BBB is disrupted.^{4,11,41} Radiotherapy has been proposed to disrupt the BBB in humans, potentially allowing antigen presenting cells or CD8+ T-cells to cross between intracranial and extracranial compartments. Additionally brain tumors themselves may disrupt the BBB (Figure 2).^{42–44} It is possible that both these mechanisms are needed for an abscopal effect to occur. This was corroborated by Grimaldi et al.²², where 85% of patients with an abscopal effect showed local tumor response to radiotherapy, implying a relationship between intracranial response (tumor death) and distant tumor effect. Last, while not included in our study, there was one case report where a patient with glioblastoma (GBM) had a drug sensitivity reaction five days following radiation therapy (and with no concurrent systematic therapy). While there was no secondary tumor foci in this patient for an abscopal effect to occur, it supports permeability of the BBB and a heightened immune response following radiotherapy.⁴⁵

While most cases in our review present an extra-cranial response to intra-cranial radiation, Piercy et al.¹¹ describes an intracranial response after radiation targeted to the axilla, suggesting that the abscopal effect may potentially be harnessed following systemic treatment. Conversely, Ishiyama et al.¹⁶ reported a case of continued intracranial tumor progression despite the presence of an abscopal effect at other sites of

systemic disease, therefore arguing the brain remained a privileged site in this case. Finally, it has been proposed that alternative, parallel systems of drainage and communication from the brain to the systemic circulation (e.g. “glymphatics”) may be a potential source of antigen presentation.⁴⁶

Ultimately, the abscopal effect has significant implications for neurosurgeons, neuro-oncologists, radiation oncologists, and those treating patients with brain or spine metastases. Further study is needed on those pathologies particularly susceptible to the abscopal effect, optimal timing of radiation and systemic therapeutics, radiation-delivery platforms which are more likely to induce the abscopal effect, and the effect of concurrent immunotherapy.

Limitations

There are multiple limitations to the current study. The largest limitation is that it consists primarily of case reports, which cannot be easily generalized. Second, there are multiple confounders within the treatment modalities of the patients analyzed, including concurrent systematic therapies, timing of radiotherapy, frequency, and accuracy of follow-up, etc. In addition, smaller changes in tumor size may be driven by similar immunogenic mechanisms as an abscopal effect but may not be classified as such compared to the large, dramatic reductions in tumor size as often reported in the case series identified. Finally, this review is subject to the limitations of all systematic reviews, including publication bias and non-standardized reporting of treatment and outcomes. Nonetheless, we believe the growing interest in this topic presented a unique opportunity to discuss the abscopal effect through case reports and small case series as it pertains to the practicing neurosurgeon-oncologist.

Conclusion

The abscopal effect is a rare phenomenon but is well documented. Patients receiving radiotherapy to the brain or spine for metastatic disease and on immune checkpoint inhibitor therapy may benefit from a heightened immunologic response and regression of tumors distant to the irradiated site. Further investigation into the role of the blood–brain barrier, treatment strategies, and stratified patient populations most likely to benefit from the abscopal effect are necessary.

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