Advances in Radiation Oncology (2020) **5**, 444-449

advances
in radiation oncology

www.advancesradonc.org

Scientific Article

Outpatient Anesthesia Facilitates Stereotactic Body Radiation Therapy for Early Stage Lung Cancer Patients With Advanced Cognitive Impairments

Senthilkumar Gandhidasan, MD,[a] Chandana A. Reddy, MS,[b] Neil M. Woody, MD,[b] Kevin L. Stephans, MD,[b] Molly Freeman, CNP,[b] and Gregory M.M. Videtic, MDCM, FRCPC, FACR, FASTRO[b,*]

[a]Department of Radiation Oncology, Illawarra Cancer Care Centre, Wollongong, NSW, Australia; and [b]Department of Radiation Oncology, Taussig Cancer Centre, Cleveland Clinic, Cleveland, Ohio

Received 27 August 2019; revised 23 September 2019; accepted 23 September 2019

Abstract

Purpose: To report on the use of outpatient anesthesia (OPA) facilitating delivery of stereotactic body radiation therapy (SBRT) in patients with severe cognitive impairments (CI) diagnosed with inoperable early stage lung cancer.

Methods and Materials: We surveyed our institutional review board−approved prospective lung SBRT data registry to document the feasibility of using anesthesia in CI patients and to determine their SBRT outcomes.

Results: From 2004 to 2018, 8 from a total 2084 patients were identified for this analysis. The median age at treatment was 68 years (range, 44-78). Most patients were female (62.5%). CI diagnoses included Alzheimer-related dementia (3 patients), chronic schizophrenia (3 patients), severe anxiety disorder (1 patient), and severe developmental disability (1 patient). The median tumor size was 3.4 cm (range, 1.1-10.5), and 7 patients (87.5 %) had central lesions. The median follow-up time was 22.5 months. The most common (50%) SBRT schedule used was 50 Gy in 5 fractions. Intravenous propofol (10 mg/mL) was used for OPA in all cases at the time of simulation and with daily treatments. OPA was well tolerated and all patients completed SBRT as prescribed. There was one grade 5 but no other grade 3 or higher SBRT-related toxicities. One patient died with local failure and one of distant failure.

Conclusions: OPA made lung SBRT feasible for patients with CIs. SBRT outcomes were in keeping with those reported in the literature. CI should not be considered a contraindication per se to SBRT delivery in patients otherwise appropriate for this modality.

Introduction

During the past 2 decades, lung stereotactic body radiation therapy (SBRT) has emerged as the standard of care for the curative management of patients with early stage nonsmall cell lung cancer (NSCLC) who are

Sources of support: none.
Disclosures: none.

* Corresponding author: Gregory M.M. Videtic, MDCM, FRCPC, FACR, FASTRO; E-mail: videtig@ccf.org

https://doi.org/10.1016/j.adro.2019.09.009

considered inoperable owing to their medical comorbidities.[1] A broad range of studies, including randomized trials showing its superiority compared with conventional fractionated radiation therapy, has shown that it provides excellent cancer control with minimal treatment-related toxicities.[1-4]

To ensure accurate delivery of very high doses to a target in the lung while avoiding normal structures, SBRT requires rigid patient immobilization, means of respiratory motion management and analysis, and daily image guidance for treatment verification.[5] In addition, patients undergoing SBRT must have the necessary physical and mental competencies to participate in complex processes that may extend over long periods of time. For example, patients may be expected to lie still for lengthy periods in body molds while tolerating restricted breathing due to external abdominal compression and do this without becoming agitated or uncooperative.

Patients unable to participate fully and voluntarily in their care therefore present a difficult clinical problem because the ability to deliver safe and effective radiation becomes compromised.[6] That is why children often present special concerns as a function of their age while undergoing radiation therapy.[7,8] For children who cannot be safely or repeatedly immobilized on their own, anesthesia or sedation can be used to sedate them for both simulation and each subsequent treatment.[6-9] The feasibility and safety of general anesthesia or sedation given to children for the purposes of daily radiation therapy is well documented in the literature. For example, the use of anesthesia to support cranial radiosurgery in the pediatric population is well established.[9,10]

In contrast to the pediatric literature, there are few clinical reports on the appropriateness of anesthesia in adults undergoing radiation therapy. In addition to its recommended use for combative or confused patients,[6] other relevant clinical scenarios where sedation might play a role could include severe pain syndromes, claustrophobia, chronic anxiety disorders, or advanced neuromuscular disabilities. In view of the paucity of such reports the aim of the present study was to present our institutional experience in treating otherwise clinically stable patients with early stage inoperable lung cancer who had cognitive impairments (CIs) that compromised their ability to tolerate the routine procedures and processes associated with lung SBRT and that then necessitated the use of outpatient anesthesia (OPA).

Methods

For this retrospective review, we surveyed our institutional review board–approved SBRT prospective registry from April 2004 until December 2018 for any American Joint Committee on Cancer, seventh edition,[11] early-stage lung cancer patients requiring anesthesia or sedation at the time of treatment. All patients had been judged as medically inoperable by an experienced thoracic surgeon, or within the setting of the institutional multidisciplinary thoracic tumor board. All patients were staged with computed tomography (CT) scans of the chest and positron emission tomography (PET). Imaging of the brain (by magnetic resonance imaging or CT) was carried out at the discretion of the treating physician on the basis of patient- or tumor-specific factors. If the PET imaging showed no mediastinal nodal hypermetabolic activity, mediastinoscopy or bronchoscope-guided ultrasound nodal sampling were not required. As per previously published practice,[12,13] patients with nonbiopsied or nontissue-typed but highly PET-avid lung lesions that had demonstrated growth on serial CT imaging of the chest were labeled as clinical or radiographic early stage malignancy and were treated with lung SBRT.

Pretreatment evaluation included a complete history and physical examination and after that assessment anesthesia would be recommended for those patients who displayed severe cognitive or psychologic disturbances that were not compatible with safe execution of lung SBRT processes. The anesthesia records relevant to each patient were also reviewed for this analysis. Figure 1 describes our institutional flowchart in carrying out OPA-based lung SBRT. All patients had an anesthesiology consult before using OPA for SBRT and all treatments were initiated, administered, and monitored on site in the radiation oncology department by the anesthesia team. OPA consisted of propofol, 10 mg/mL-based intravenous (IV) sedation regimen in all cases. The patient was sedated at the time of simulation and then daily before treatment. Patient respiratory status was monitored and controlled throughout by the attending anesthetist. Patients were recovered postanesthesia in the department and discharged home the same day. No major interventions such as telemetry or bladder catheterization were required.

At the time of simulation, immobilization involved a vacuum bag restriction system (Bodyfix, Medical Intelligence Inc, Montreal, Quebec, Canada). Tumor motion management in all cases involved application of an abdominal compression device designed to limit the maximum range of tumor motion to <1 cm in all directions. Thereafter, confirmatory 4-dimensional CT simulation with a Philips (Philips Health care, Andover, MA) bellows device was carried out. Treatment planning was carried out with BrainLAB planning software until 2013 and then with Pinnacle-based software. Following Radiation Therapy Oncology Group lung SBRT protocol definitions,[14] individualized gross tumor volumes and internal target volumes were created from CT simulation

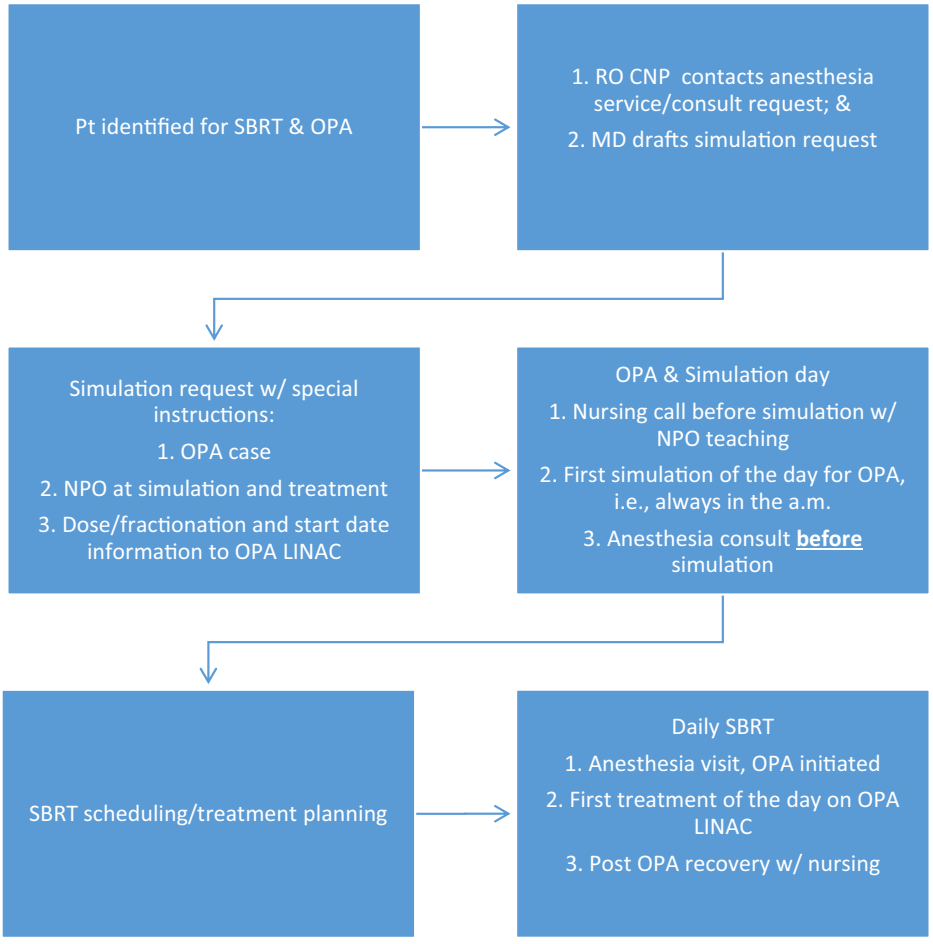

Figure 1 Flowchart for lung SBRT and OPA. *Abbreviations*: CNP = certified nurse practitioner; LINAC = linear accelerator; MD = physician; NPO = nothing by mouth; OPA = outpatient anesthesia; Pt = patient; RO = radiation oncology; SBRT = stereotactic body radiation therapy.

studies, with clinical target volumes not required for planning. A 5-mm fixed expansion of the internal target volumes generated the planning target volume in all cases.

Lung SBRT dose/fractionation selection for a given patient was at the discretion of the treating physician and reflected the treatment era, tumor location, and experience derived from participation in clinical trials. A tumor's location was characterized as either peripheral or central per the definitions of the Radiation Therapy Oncology Group.[14]

With respect to treatment platform, the majority of patients were treated principally on Novalis-BrainLAB systems (Varian Medical Systems Inc, Palo Alto, CA; BrainLAB AG, Feldkirchen, Germany), and a Varian Edge system (Varian Medical Systems Inc, Palo Alto, CA) since 2013.

Results

Of 2084 patients treated with lung SBRT during the interval of interest, 8 (0.4%) required OPA for their treatment owing to a concurrent severe CI. The forms of CI seen in this cohort were Alzheimer's dementia (37.5%), chronic schizophrenia requiring institutionalization (37.5%), severe anxiety disorder (12.5%), and severe mental disability from birth with permanent tracheostomy (12.5%). All patients tolerated the sedation process. One patient developed hypotension during his initial sedation which was successfully managed and subsequent OPA was administered without complications. There were no unusual adverse reactions to the use of OPA during treatment, which modified its use during SBRT sessions, and no delayed complications were observed. All patients were able to complete their courses of SBRT without interruption.

Table 1 provides a summary of selected patient, tumor and treatment characteristics. The majority of patients was female (62.5%), the median age 68 years (range, 44-78), and the median Karnofsky performance status 70 (range, 40-80). The median body mass index was 24 (range, 19.5-27.7). Five patients (62.5%) completed spirometry: median forced expiratory volume in 1 second (FEV_1) was 1.34 L (range, 0.63-1.62) and 44% predicted (range, 24-

Table 1 Selected patient, tumor, and treatment characteristics of 8 medically inoperable NSCLC patients treated with SBRT and outpatient anesthesia

Patient	Year of SBRT	CI	Sex	Age at SBRT	Smoking at SBRT?	KPS	BMI	Previous lung cancer, year	Selected comorbidities of interest	T (cm)	Histology	Central per RTOG 0236	AJCC 7th ed. stage	Tumor PET SUVmax	SBRT dose/fx
1	2006	MD	M	44	NS	60	26.8	N	-	3.0	Sq	Y	IA	9	50/10
2	2013	AD	F	77	Y	80	19.5	Y, 2012	COPD	1.7	Sq	Y	IA	10.5	50/5
3	2014	SCZ	M	70	N	70	25	N	-	5.8	Sq	Y	IIA	11	60/8
4	2014	AD	F	78	N	70	27.7	Y, 1992	CAD, CTD, CVD, CKD	3.8	Sq	Y	IB	9	50/5
5	2015	SCZ	F	66	Y	70	22.4	N	COPD, CHF, CAD, HTN	3.0	Sq	Y	IA	25.5	50/5
6	2016	SCZ	F	55	N	80	22.9	N	COPD, HTN, CKD	10.5	Sq	Y	IIIA	6.4	60/8
7	2016	AD	F	66	Y	70	25.1	N	COPD, DM, HTN	5.0	Sq	Y	IB	14.8	50/5
8	2017	AX	M	73	N	70	23	N	CAD, CHF, CVD, HTN	1.1	NB	N	IA	8.6	34/1

Abbreviations: AD = Alzheimer's dementia; AX = severe anxiety disorder; BMI = body mass index; CAD = coronary artery disease; CI = cognitive impairment; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CTD = connective tissue disorder; CVD = cerebrovascular disease; DM = diabetes mellitus; F = female; fx = fraction; HTN = hypertension; KPS = Karnofsky Performance Status; M = male; MD = mental disability; N = No; NB = nonbiopsied; NS = never smoker; RTOG = Radiation Therapy Oncology Group; SBRT = stereotactic body radiation therapy; SZC = chronic schizophrenia; Sq = squamous cell carcinoma; SUVmax = maximum standardized uptake value; T = tumor maximal diameter; Y = yes.

82); only 3 (37.5%) were able to complete diffusion capacity testing. Three (37.5%) were smoking at treatment time. The median tumor diameter was 3.4 cm (range, 1.1-10.5). The median PET SUVmax was 9.75 (range, 6.4-25.5). Seven patients (87.5%) had a central tumor and squamous cell cancer histology.

The median follow-up time was 22.5 months. At analysis, 3 patients (37.5%) had died. The median overall survival for the cohort was 38.2 months. In terms of toxicity, one patient (patient in Table 1) died of a grade 5 tracheoesophageal fistula in the absence of cancer at 8.2 months after SBRT. Otherwise there were no grade 3 or higher toxicities. Concerning patterns of failure, one patient (12.5%) died with biopsy-proven loco-regional failure 105.7 months after SBRT and 1 patient (12.5%) failed distantly. Otherwise, there has been no other local, regional nodal, or distant failure at the time of analysis.

Discussion

To our knowledge, this is the first reported series describing the use of OPA to make SBRT feasible in treating medically inoperable early stage NSCLC patients with severe CI. Reporting on this novel although small series is intended to encourage clinicians to broaden the range of high-risk patients they might consider for SBRT. With respect to the parameters of SBRT, patients completed their prescribed regimens without interruptions or alterations. Sedation permitted maximal application of compression to manage motion without discomfort to patients. The degree of compression was also supported by the continuous supervision of the respiratory status by the anesthesia team and therefore allowed optimal restriction of tumor motion, generating the best achievable planning target volume for planning. Even for such a small sample size, the present results are in keeping with outcomes expected from SBRT for medically inoperable early-stage NSCLC[1] and more specifically, given their preponderance in this cohort, for central lung tumors.[15] In that regard, the patient who had a grade 5 toxicity had a 5.8 cm central tumor of the right upper lobe of the lung abutting a segment of the esophagus. This toxicity occurred, unfortunately, despite selecting an SBRT schedule of 60 Gy in 8 fractions used for higher risk central tumors as well as optimizing planning with respect to avoiding circumferential dose to the esophagus.

This report adds to the existing literature (which has been essentially pediatric) on the use of sedation in the delivery of radiation therapy, but now does so in the context of adult medicine. Furthermore, as with OPA for pediatric radiosurgery, it validates the use of propofol-based OPA for the effective and complete delivery of complex, curative SBRT. Agents such as propofol have very low complication rates owing to improved drug side effect profiles, hence it is one of the most common agents

used in outpatient anesthesia,[4,10] and this was validated by our experience. For example, from a multi-institutional survey of anesthetic practices at proton therapy centers, intravenous propofol was the most commonly used anesthetic agent to ensure prolonged immobilization during pediatric treatment sessions.[16] Inasmuch as propofol in our series was the sole agent chosen for our outpatient procedure, the choice of anesthetic ultimately must be determined by the anesthetic provider after examining the patient and reviewing the patient's medical history. Critical to that decision is the knowledge that radiation therapy is a painless procedure and therefore deep sedation or general anesthesia is not required. Propofol has a rapid onset and offset of action and reduced incidence of delirium or emergence agitation, particularly important for those patients with CI. Relevant drug complications to lung SBRT treatments may include respiratory complications (airway obstruction, broncho/laryngospasm, desaturation), cardiovascular complications (arrhythmias, hypotension), nausea, and vomiting.[8] Duke University Medical Center reported on their use of propofol induction followed by inhalational maintenance in 123 pediatric patients treated with external beam radiation therapy and noted that their rate of complications due to the anesthetic were very low at 1.3%.[17]

From a process perspective, our use of OPA was facilitated by a dedicated institutional outpatient anesthesia service and an active pediatric radiation oncology practice using sedation routinely. We therefore benefited from experienced staffing and expertise on integrating OPA into linear accelerator utilization. Clinicians have to recognize the additional challenges when using OPA, as it bears on human and time resources, equipment setup, and monitoring and having access to a supportive and experienced anesthesia service. The latter need may then limit OPA use to primarily high-volume or hospital-based academic centers. The use of anesthesia with radiation therapy also adds several layers of complexity to the delivery of treatment. This includes anesthesia risks, increased treatment delivery time, requirement of an anesthesia recovery team and space, increased cost owing to anesthesia billings, and scheduling constraints on the entire department owing to patient NPO needs requiring early treatment.[8,18]

Overall, one can argue that using anesthesia to facilitate SBRT in the setting of cognitive impairment follows the same rationale justifying the treatment for any inoperable early stage lung cancer patient. As shown by McGarry et al, observation only for inoperable patients with early stage lung cancer is associated with poor outcomes, with more than 50% dying from lung cancer rather than competing causes of death.[19] The potential morbidity of untreated lung cancer in any population cannot then be ignored.

Conclusions

OPA made lung SBRT possible for medically stable but inoperable lung cancer patients with severe CIs. SBRT outcomes were in keeping with expected values reported for medically inoperable lung cancer patients. Therefore, cognitive or psychological impairments should not be considered relative contraindications to choosing lung SBRT in patients otherwise appropriate for this modality, provided resources to administer anesthesia are available.

References

1. Videtic GMM, Donington J, Giuliani M, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. *Pract Radiat Oncol*. 2017;7:295-301.
2. Potters L, Kavanagh B, Galvin JM, et al, American Society for Therapeutic Radiology and Oncology; American College of Radiology. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guideline for the performance of stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2010;76:326-332.
3. Nyman J, Hallqvist A, Lund JÅ, et al. SPACE: A randomized study of SBRT vs conventional fractionated radiotherapy in medically inoperable stage I NSCLC. *Radiother Oncol*. 2016;121:1-8.
4. Ball D, Mai GT, Vinod S, et al. Trans Tasman Radiation Oncology Group 09.02. CHISEL investigators stereotactic. *Lancet Oncol*. 2019;20:494-503.
5. Kolker A, Mascarenhas J. Anesthesia for outfield procedures in cancer patients. *Curr Opin Anesthesiol*. 2015;28:464-468.
6. Tsang RW, Solow HL, Ananthanarayan C, Haley S. Daily general anesthesia for radiotherapy in unco-operative patients: Ingredients for successful management. *Clin Oncol (R Coll Radiol)*. 2001;13:416-421.
7. Latham GJ. Anesthesia for the child with cancer. *Anesthesiol Clin*. 2014;32:185-213.
8. Verma V, Beethe AB, LeRiger M, Kulkarni RR, Zhang M, Lin C. Anesthesia complications of pediatric radiation therapy. *Pract Radiat Oncol*. 2016;6:143-154.
9. Stokes MA, Soriano SG, Tarbell NJ, et al. Anesthesia for stereotactic radiosurgery in children. *J Neurosurg Anesthesiol*. 1995;7:100-108.
10. Owusu-Agyemang P, Grosshans D, Arunkumar R, et al. Noninvasive anesthesia for children undergoing proton radiation therapy. *Radiother Oncol*. 2014;111:30-34.
11. Lung. In: Edge SB, Byrd DB, Compton CC, Fritz AG, Greene FL, Trotti A, eds. *AJCC Cancer Staging Handbook*. 7th ed. New York, NY: Springer; 2010:209-323.
12. Stephans KL, Djemil T, Reddy CA, et al. A comparison of two stereotactic body radiation fractionation schedules for medically inoperable stage I non-small cell lung cancer: The Cleveland clinic experience. *J Thorac Oncol*. 2009;4:976-982.
13. Nyman J, Johansson KA, Hulten U. Stereotactic hypofractionated radiotherapy for stage I non-small cell lung cancer—Mature results for medically inoperable patients. *Lung Cancer*. 2006;51:97-103.
14. Bezjak A, Paulus R, Gaspar LE, et al. Efficacy and toxicity analysis of NRG Oncology/RTOG 0813 trial of stereotactic

body radiation therapy (SBRT) for Centrally located non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys*. 2016;96:S8.
15. Senthi S, Haasbeek CJ, Slotman BJ, Senan S. Outcomes of stereotactic ablative radiotherapy for central lung tumours: A systematic review. *Radiother Oncol*. 2013;106:276-278.
16. Owusu-Agyemang P, Popovich SM, Zavala AM, et al. A multi-institutional pilot survey of anesthesia practices during proton radiation therapy. *Pract Radiat Oncol*. 2016;6:155-159.
17. Fortney JT, Halperin EC, Hertz CM, Schulman SR. Anesthesia for pediatric external beam radiation therapy. *Int J Radiat Oncol Biol Phys*. 1999;44:587-591.
18. McMullen KP, Hanson T, Bratton J, Johnstone PA. Parameters of anesthesia/sedation in children receiving radiotherapy. *Radiat Oncol*. 2015;10:65-69.
19. McGarry RC, Song G, des Rosiers P, Timmerman R. Observation-only management of early stage, medically inoperable lung cancer: Poor outcome. *Chest*. 2002;121:1155-1158.