

Stereotactic Body Radiation Therapy: A Review of Applications and Outcomes

Rajeev Pandey^{1,4*}, Gurumurthy^{2,4}, Jesse Galinski^{3,4}, Andrew Haddad^{3,4} and Payal Dhaduk^{3,4}

¹Department of Biochemistry, Spartan Health Sciences University School of Medicine, St. Lucia, West Indies

²Department of Neurosciences, Spartan Health Sciences University School of Medicine, St. Lucia, West Indies

³Medical Students, Spartan Health Sciences University School of Medicine, St. Lucia, West Indies

⁴Department of Radiation Oncology, Community Health and Research Center of Spartan (CHARCOS), Summa Cancer Institute, 161 North Forge Street, Akron, Ohio, USA

*Corresponding author: Rajeev Pandey, Associate Professor, Department of Biochemistry, Spartan Health Sciences University, PO Box 324, St. Lucia, West Indies, Tel: (718) 454-6126; Fax: (718) 454-6811; E-mail: rpandey@spartanmed.org

Received date: Mar 18, 2015, Accepted date: May 29, 2015, Publication date: June 02, 2015

Copyright: © 2015 Pandey R, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Radiotherapy is a versatile tool used in the treatment of various types of benign and malignant neoplasms. However, conventional radiation therapy for cancerous conditions often results in collateral damage to healthy tissues due to involvement of oversized radiation fields. Over the last decade one type of precision based radiation treatment has developed. This new treatment, known as Stereotactic Radiosurgery (SRS), involves highly accurate beams of high-energy radiation that are used to destroy abnormal cells by permanently damaging their DNA. As technology progressed stereotactic cranial radiosurgery developed into a successful method for certain tumorous conditions of the head and skull. The success of stereotactic cranial radiosurgery led to further radiation application research to widen the spectrum of treatable conditions to include those located extracranially. The result of this continued research led to the development of stereotactic body radiation therapy (SBRT), a radiotherapy technique based upon principles of SRS that is used to treat small or moderate sized tumors of the body with a limited number of treatments. Stereotactic body radiation therapy combines the use of the latest tumor imaging technology as well as precision based radiation delivery mechanisms to overcome physiological barriers of normal radiation therapy such as movement of tumors in tissues. The net effect of SBRT is that a dose of radiation much larger than normal can be administered in a very precise manner, over smaller time frame, bringing about a dramatic tumor response. In this review the authors will attempt to briefly cover the subject of stereotactic body radiation therapy as well as its applications and effectiveness.

Keywords: Stereotactic body radiation therapy; Extracranial radiation therapy; Radiation therapy organ motion

Introduction

The term “Stereotactic” refers to a procedure in which the targeted mass is localized in relation to a fixed three dimensional reference system such as a rigid head frame, cranial landmarks, or fixed artificial markers. “Radiosurgery” refers to the use of radiation to destroy cancerous cells with the total number of treatments being five or less [1]. Thus, Stereotactic Radiosurgery, (SRS), is recognized as a discipline that relies on the use of ionizing radiation to inactivate or destroy neoplastic cells of distinct targets located within the head or spinal column with the total number of treatments being less than or equal to five. Localization and treatment of masses via this system involves physicians performing image-guided, radiological procedures with an extremely high degree of accuracy and precision. The main two benefits garnered via SRS over conventional radiation treatment are that 1) large fields of radiation that damage normal tissues are not involved and 2) the entire procedure is non-invasive and does not require the additional health protocols associated with invasive or minimally invasive procedures. Coupling the latest tumor imaging technology with precisely positioned anatomic or artificial reference points allows the use of high dose radiation that maximizes the ablative effect on the targeted mass while limiting damage to non-targeted tissues. SRS, therefore, represents an alternative choice for

many patients seeking treatment for cranial neoplastic conditions. Since the induction of Stereotactic Radiosurgery literally thousands of publications have been written on the basis of its clinical use and benefit to patients in treating various cancerous conditions. The majority of these studies focus on radiosurgery as it applies to the treatment of conditions involving intracranial or spinal masses. SRS is currently used as management for conditions such as metastatic and primary, malignant, intracranial or central nervous system tumors, as well as benign tumors like acoustic neuromas, meningiomas, and pituitary adenomas. SRS is also a treatment option for arterio-venous malformations and functional neuropathic pain disorders such as trigeminal neuralgia. The advancement of recent medical technologies has paved the way for the development of various treatment options involving SRS as well as other branches of radiotherapy.

The success of SRS technology led many to question if a radiosurgical technique could be developed that operated under the basic principles of SRS with the exception that the procedure would be used on the body as opposed to the head. The result of further research and development was the introduction of Stereotactic Body Radiation Therapy, (SBRT). Essentially, SBRT is the novel application to SRS for extracranial tumors. SBRT is a non-invasive radiological procedure used to treat primary and metastatic tumors in various types of tissues throughout the abdominopelvic and thoracic cavities as well as the spinal column. The major contributing factor that makes SBRT, like SRS, such an effective treatment, versus normal radiotherapy, is that SBRT involves delivery of larger than normal doses of radiation, in

only a few fractions, which results in a higher biological effective dose of radiation that has shown drastic cancer response. The method of delivery of a much larger dose is coupled to the fact that with SBRT multiple beams of radiation are focused precisely on the target tissue resulting in an additive dose of radiation to a specific area. Again, the implementation of this specific type of therapy requires the use of precision based techniques that account for physiological movement as well as the latest tumor imaging technology. SRS and SBRT reside in a category of radiation treatments known as Image Guided Radiotherapy, IGRT. SRS and SBRT are similar to Intensity Modulated Radiotherapy, IMRT, with the exception that SRS and SBRT operate on the basis of superb imaging, accuracy, and precision delivery technologies.

Application of SBRT in Treatment of Various Cancers

SBRT for NSCLC

Patients with primary or metastatic lung, liver, and spinal tumors make up the majority of patients treated via SBRT although other types of cancer can be treated [2]. Lung cancer is one of the leading causes of mortality in adults and is listed ahead of bowel, breast, and prostatic cancers in women and men with the most common presentation being adenocarcinoma, or the non-small-cell type, (NSCLC). Using SBRT, effective treatment for tumors with cross sectional diameter of up to 7 cm has been reported successful [2]. However, most specialists have limited treatment eligibility to those patients with tumors having diameters of 5 cm or less due to excellent observed outcomes. Senan et al. reported that local control rates in NSCLC were higher than 90% when patients with tumors 5 cm or less underwent SBRT [3]. Baumann et al. in a phase II trial reported that patients with medically inoperable NSCLC treated with SBRT had cancer specific survival rates at 1, 2, and 3 years of 93%, 88%, and 88% respectively [4]. According to the American Lung Association almost three quarters of patients with lung cancer have advanced disease at presentation, and many of these have had symptoms for many months [5,6]. Early diagnosis and prompt referral are therefore major priorities. In a publication detailing the five year experience of a single institution Zhang et al. reported a 25% overall survival rate at 5 years after undergoing SBRT as a treatment for multiple metastatic NSCLC tumors [7]. Participants in the above study were 71 in number had a combined total of 172 metastatic lesions treated with SBRT from 2000-2006. All of the patients included in the study failed after surgery and/or chemotherapy previous to undergoing SBRT. The median dose of radiation used was 48 Gy given in 4 fractions to lesions with a median size of 2.1 cm. Zhang et al. concluded that SBRT should be an alternative treatment for metastatic lung tumors with favorable long term survival rates and minimal complications [8]. Grills et al. reported that there was no difference in regional recurrence, distant metastasis, or freedom from failure at 30 months post procedure in patients who had NSCLC who underwent wedge resection vs. SBRT. The only difference reported by Grills was that overall survival rates were higher with wedge resection but cause specific survival rates were identical to those of SBRT [7]. The overall effect of SBRT on 1A and 1B primary NSCLC in Japanese patients can be judged by comparing SBRT CSS rates of 72-62% at 5 years to CSS lobectomy rates of 100-57% at 5 years, depending on size of the primary tumor [9]. In view of the above, SBRT appears to be a highly effective, non-invasive treatment for lung cancers that are primary, metastatic, operable, or inoperable.

SBRT for liver cancers

SBRT has emerged as a favorable treatment option for hepatic cancers. Numerous studies have been conducted concerning the use of SBRT for liver cancers, all of which demonstrate positive results. Radiotherapy treatment of the liver is challenging process due to respiratory motion and radiosensitivity of the organ. Developments in radiation technology such as image guided radio therapy (IGRT) and SBRT have allowed for increasing precision radiation delivery and improved liver cancer survival rates [10]. More specifically, hypofractionated SBRT provides excellent local control with minimal side effects in selected patients with limited hepatic metastases [11]. Ada Law and her colleagues conducted a study on 33 patients with hepatocellular carcinoma. The results of her study showed that after a median follow-up period of 16.5 months (range: 3.5-40.7), all but 2 patients demonstrated radiological tumor regression. Eight patients (24%) achieved complete remission [12]. Another study conducted by Hualin Zhang and fellow colleagues assessed survival rates for patients recovering from SBRT for liver cancers. Results were promising showing that 1,2 and 3 year overall survival rate estimates are 100% (95% CI: 100-100%), 91% (95% CI: 51-99), and 64% (95% CI: 22-87), respectively [13]. The use of high dose radiation for hepatic cancer has drawn concern for liver toxicity and decreased liver function. However studies have shown that with a low 90 day mortality rate (5.5%), and no clinically relevant impact on liver function, SBRT offers a safe adjuvant treatment option for this patient population [14]. The above studies, among many others, continue to suggest that SBRT is not only safe but also successful in the treatment of hepatic cancers.

SBRT for spinal column tumors

One of the major applications of SBRT that has recently emerged is the treatment of primary or metastatic spinal column tumors. Spinal metastasis are one of the most common occurrences in patients with advanced stages of cancer. Spinal SBRT is an excellent high dose treatment for tumors that have been previously treated with other types of radiotherapy [15]. The advantage of SBRT on the spinal column is that the precision involved in the procedure minimizes the chance of radiation damage to the spinal cord while effecting maximum tumor radiation response and preventing spinal cord compression [16]. Spinal SBRT, however, is a more complex procedure due to the frequent occurrence of spinal tumors in close proximity to delicate CNS structures. SBRT for the spine has most often been used for metastatic tumors less than three adjacent vertebral bodies in length, and when a tumor is at least 1-2 mm away from the spinal cord in order to avoid underdosing or missing epidural disease [17]. Normally, spinal SBRT procedures are well tolerated, however, transient pain in the form of acute pain flare has been shown to be a side effect of SBRT which must be discussed with patients undergoing the procedure [18]. Long term complications can result in vertebral compression fractures and even possible paralysis due to myelopathy. Hubert et al. conducted a survey of radiation oncologists on the use of SBRT and reported the following: Spinal tumors were the second most treated tumors with 67% of reporting physicians utilizing SBRT technology for treatment of spinal tumors. The most commonly reported number of radiation fractions used for treatment of primary or metastatic spinal tumors was 1, and for single fraction regimens the most common Gy doses were 16 or 18. Interesting to note, Hubert also reported that among SBRT nonusers, the most common reason for nonuse was lack of SBRT equipment and

that 66.5% percent of nonusers planned to adopt SBRT due to its specific benefit [19].

The essential apparatus required for spinal SBRT can be acquired through different commercially available or institution-specific systems. Several systems are currently available each of them utilizing slightly different techniques and methods for accurately delivering spinal radiation doses. Two of the more common systems are detailed below. CyberKnife, (Accuray, Inc., Sunnyvale, CA) is a frameless robotic radiosurgical system that plays an important role in spinal radiosurgery. The CyberKnife setup consists of a lightweight linear accelerator (LINAC) mounted on a robotic manipulator that serves to deliver several independent non-isocentric and non-coplanar radiation beams. Deliverance of radiation is tailored to periodic X-ray imaging with corresponding micro-adjustments in the positioning of the robotic arm to maintain accuracy of treatment. Much like the Cyberknife, the Novalis system, (Brainlab) is equipped with in-room kilovoltage X-ray imaging equipment composed of two orthogonally mounted 80–100 kiloelectron volt (keV) X-ray tubes with corresponding amorphous silicon digital detectors linked to a computerized control and image system. The acquired keV images combined with the images from CT simulation to ensure appropriate patient position. The information regarding the targeted neoplasm is forwarded to the ExacTrac system, a computerized system that uses two infrared cameras to detect infrared-sensitive markers. This allows the system to automatically compare this marker information with reference information to move the treatment couch to the desired position [20]. Gill et al. commenting on local control and toxicity of SBRT of single vertebrae spinal tumors reported that a doses of 30-35 Gy were given via Cyberknife technology, and at 34 months median follow-up (IQR, 25-40 months) for surviving patients, the 1- and 2-year Kaplan–Meier local control estimates were 80 and 73%, respectively [21]. In effect, SBRT for primary or metastatic spinal column cancers is a noninvasive procedure with excellent control rates that is being widely adopted by radiation oncologists across the United States.

SBRT for other cancers

As the application of SBRT has expanded to various other types of cancers it has continued to show major benefits in tumor reduction while minimizing unwanted side effects. For example, SBRT has shown to have promising results in cancers of the pancreas, prostate, and kidney. The pancreas presents many challenges for standard radiotherapy due to its anatomical location. The pancreas is closely positioned along the curve of the duodenum. Delivery of even moderate doses of radiation (more than 50 Gy in 1.8-2 Gy/day fractions) to the small bowel is associated with a high risk of ulceration, bleeding, and perforation [22]. The use of SBRT allows for direct regional control, a feature not applicable to other systemic therapies. In SBRT, multiple non-coplanar fixed beams or arc fields are used in order to minimize normal tissue exposure and provide rapid fall-off of the radiation dose outside of the target area [23]. This precision of treatment is necessary to avoid toxicity to surrounding organs such as the duodenum. Another complication of pancreatic cancer is that the pancreas can move with respiration and gastrointestinal peristalsis. However, SBRT can be used to treat tumors in moving tissues due to that fact that SBRT involves sub-centimeter precision [24]. Simply put, SBRT is a promising emerging method of treatment for pancreatic cancer. The prostate is also an organ in which position and movement have presented difficulties for previous radiation techniques. As noted above the Cyberknife system allows for

real-time organ position and motion corrections during radiation delivery by tracking the positions of three to four gold fiducial seeds placed in the prostate prior to treatment. These implanted seeds improve conformal isodose profiles and dose volume histograms (DVH) and enable the performance of hypofractionated SBRT for prostate cancer [25]. In terms of toxicity, studies have shown that SBRT has minimal toxic effects on the prostate. Filippo Alongi and his colleagues conducted a study to assess toxicity post SBRT in patients with prostate cancer. The results of the study indicated that no acute G3-5 was found in the trial and out of trial patients and results of the study indicate that all patients were at grade 2 toxicity or lower [26]. Various tissues of the body have early and late responses to radiation therapy of a given dose. This early or late response may present a problem in a treatment regimen as late responding tissues may require more radiation than early responding tissues. Examples of early responding tissues are tissues that rapidly divide such as skin and gut epithelium, while the prostate is an example of a late responding tissue [27]. Concerning the use of high dose SBRT for treatment of prostate cancer, in the 6th edition of Perez and Brady's Principles and Practice of Radiation Oncology, Perez and his colleagues concluded: "Applying the LQ model-based assumptions and interpretation, the α/β ratio for prostate cancer has been estimated to be very low, likely in the range of 1.5 to 3.0 Gy. If this estimate of α/β ratio for prostate cancer is correct, then higher doses per fraction should provide a more favorable therapeutic ratio than a conventionally fractionated regimen" [28]. This conclusion of more-is-less, when it comes to prostate cancer, is further solidified by the findings of Freeman et al. who reported that shorter doses of higher grade radiation, 35-36.25 Gy, given via SBRT for prostate cancer resulted in much greater 5-year survival rates [29].

Primary renal cell carcinoma (RCC), like cancers of the pancreas and prostate, is also a potential candidate for SBRT. In contrast to radiofrequency ablation and cryotherapy, Stereotactic ablative body radiotherapy (SABR) and stereotactic radiosurgery are capable of treating both larger tumors and those adjacent to collecting vessels and ureteric ducts. Additionally, these novel techniques are non-invasive and delivered whilst the patient is fully awake [29]. In a further study, Eldaya et al. reported toxic profiles in patients undergoing abdominal SBRT were excellent with only 1 patient showing grade 2 adrenal insufficiency [30]. Continuing studies all suggest statistical analysis that SBRT is a unique, potentially curative treatment approach for what once was considered inoperable primary RCC.

Planning and Procedure

Effective radiation Gy, imaging, and beam selection

Effective radiation dosage in SBRT is dependent upon multiple factors including the size of the cancer, target location, as well as surrounding tissues. Various body tissues can only withstand certain total doses of radiation labeled as Grey Units, (Gy). One Gy is defined as the absorption of one joule of ionizing radiation by one kilogram of matter, in this case human tissue. In view of this, SBRT is administered in fractions of the total dose that a given tissue can withstand, not to exceed the total for that tissue. The fraction amount given during treatment is usually highly variable and changes based on patient health and type of cancer being treated. Due to the highly destructive properties of ionizing radiation, SBRT administration requires precise delineation of patient anatomy and visualization of intended targets for localization during treatment delivery [2]. The three and four dimensional data provided by CT, PET, and MRI collectively assist in

identification and visualization for SBRT. Traditionally, CT scans have provided the basis for treatment planning and assessment, however, this technique is limited in its ability to identify small tumors and in the ability to differentiate scar tissue or radiation necrosis from malignancy. PET utilizes fluorine-18 deoxyglucose (FDG) to allow visualization of glucose metabolism, which is generally increased in cancer. More recently, hybrid spiral PET/CT scanners allow for both metabolic activity and precise anatomic localization to be captured in a single imaging procedure [31]. Currently, PET/CT is widely used for lung cancer, head-and-neck tumors, colon cancer, liver cancer, melanoma, lymphoma, and ovarian cancer [2]. In SBRT, sophisticated imaging is combined with multiple radiation beams, up to 254 in some instances, to deliver a high dose of concentrated radiation to the tumor. Although each individual beam is weak, the collective energy at the intersection of the beams provides high doses of radiation to the tumor [32]. In general, a larger number of beams yields better target dose conformity and dose fall-off away from the target. Also, when the number of beams used is sufficiently high, the choice of beam direction becomes less significant [2]. Recent developments in volumetric modulated arc techniques have the potential to create conformal dose distributions, achieve the required level of normal tissue sparing, and reduce treatment times, as compared to their static field counterparts [33].

Patient immobilization, physiological movement, and procedure

The entire SBRT protocol can be summed up as: Patient motion management, localization, tumor motion management, simulation, and delivery. Motion management entails that the patient is restrained in a way that complements the delivery of high dose radiation to specific areas. The foremost question that should be asked is whether or not the patient can remain in the position required for the duration of treatment. If the patient can be sufficiently immobilized, physiological movement of tumors in tissue such as in the lung can be accounted for by the radiation delivery and imaging apparatus. Several different patient immobilization devices are currently available and should be judged based on how they aid in effective radiation delivery, patient comfort, and ease of use. In a comparison between patient immobilization systems used for SBRT it was concluded that if no significant difference in tumor reduction was shown, the ideal immobilization system was the one that was more comfortable for the patient and could be set up and taken down the fastest by those administering treatment [34]. Concerning the physiological movement of tissues during patient immobilization SBRT shows a marked advantage over typical radiotherapy. The model scenario for this movement is a tumor of the lung or GI tract that moves with inhalation, exhalation, or peristalsis. Physiological shifting of the target tumor can be overcome by the use of highly detailed imaging technology such as 4D-CT scans with 1-3 mm thickness and varied breathing and restraint techniques. To ensure accurate localization and tumor motion verification patients typically undergo CT scans while breathing normally and while holding their breath. Both slow and fast CT scans are taken and used as reference points for radiation delivery boundaries. The result of combining SBRT with the latest imaging is an extremely sharp dose gradient with a tumor ablative dose drops to a safe dose within millimeters to avoid damaging non-targeted tissues. When administering radiation therapy three measures of volume are indicated. The first is the gross tumor volume, (GTV), this is essentially the visual size of the targeted tumor. The second measure of volume is the clinical target volume, (CTV), and

encompasses the microscopic spread of the tumor not visualized by imaging. The last volume considered is the planning target volume, (PTV), which allows for fluctuations in movement, dose delivery, and considers the health of surrounding tissues. Bibault et al. reported successful treatment of hepatocellular carcinoma with a median total dose of 45 Gy given in three mean fractions of 15 Gy. Tumors treated had a median diameter of 37 mm with CTVs 10 mm larger in all directions than the gross tumor volume and the PTV was 1.5 mm [33]. While analysing the shifts of lung tumors during respiration Krinski et al. reported that anterior/posterior shifts of tumors were about 1 mm on average while cranial/caudal shifts averaged about 2 mm and that the precision of SBRT was sufficient to cover tumor ablation while minimizing normal tissue to radiation exposure [35]. The processes of immobilization, visualizing the target, and ensuring accuracy of radiation delivery are essential to planning the actual delivery of radiation and are usually completed on visits to the treatment facility previous to receiving radiation. Once all imaging and immobilization data for a patient have been gathered the patient undergoes a quick simulation in the correct position to ensure accurate treatment. Upon a successful simulation the patient is ready for the actual treatment and the same procedure is repeated with delivery of radiation. Median length of treatments sessions from start to finish was reported by two separate studies as 103 minutes (range 35-156 minutes) and 109 minutes (range 36-199 minutes) [36,37]. The actual length of SBRT treatment session depends on several factors such as proper imaging, patient alignment, and type of cancer. However, slightly longer sessions lengths are offset by the reduction in number of overall treatments compared to standard radiotherapy in which treatment regimens can continue for weeks.

Post-Procedure and Recovery

The actual SBRT procedure as detailed above is relatively quick compared to standard therapy and should not normally result in patient hospitalization. Procedures usually occur at dedicated radiological oncology centers and patients are free to return home after therapy has been completed that same day. Those patients undergoing SBRT are generally free to live a normal lifestyle as they would before beginning treatment.

Although SBRT has been shown to be an effective methodology of treatment for various types of cancers, patients undergoing the procedure still retain the risk of negative side effects associated with radiation treatment. The experience of side effects due to radiation is highly variable and coincides to the overall health of the patient before treatment, the radiation dose given, and the location and stage of cancers treated. The majority of side effects occurring with radiation therapy are due to normal tissue damage from exposure to high dose radiation. Generalized fatigue, nausea, vomiting, and pain are the most commonly experienced side effects of any radiation therapy regimen. It is important to understand that the fatigue experienced from radiation therapy is not the normal fatigue due to overexertion and does not always go away with rest. The degree of fatigue experienced can fluctuate and can even be worsened if chemotherapy or surgery has also played a role in patient treatment. In most cases fatigue will spontaneously remit after radiation therapy has ceased but in some cases may persist for months afterward. Nausea and vomiting can be reduced via the use of antiemetic drugs like the 5-HT₃ receptor antagonist ondansetron. Diarrhea can be treated via diet restrictions and medication. Post radiation pain management can entail any number or combination of medications as well as physical therapy to

reduce pain and allow normal daily function. Skin problems such as dryness, peeling, or itching are another common side effect of radiation treatment and can be resolved by alteration of the dose of radiation or specific skin care. Radiation to the thoracic cavity may result in any number of side effects including difficulty swallowing, shortness of breath, cough, fever, bone fracture, and radiation pneumonitis. In follow up visits with 36 patients who had undergone chest SBRT for 38 lesions, Turzer et al. reported that 34 of the patients had grade 1 pneumonitis, 1 patient had grade 2 pneumonitis and 1 patient had grade 3 pneumonitis [38]. In the same study 16 of the 36 patients presented with temporary chest pain related to the radiation field and all symptoms of inflammation and pain reduced after three months treatment with corticosteroids, NSAIDs, and morphine [38]. Radiation therapy to the abdominal cavity most commonly resulted in diarrhea, nausea, and vomiting and is treated as stated above. In the treatment of surgically inoperable cancers of the liver with SBRT Goyal et al. determined that the side effects experienced were attributed to surgery, placement of fiducial markers, chemotherapy, radiation induced, or related to medical comorbidities with pain being a side effect induced by SBRT [39]. However, another study conducted to assess pain relief as well as toxicity following SBRT demonstrated that 3 out of 4 patients were pain free post SBRT and one had improved pain [15]. The side effects of radiation therapy to the pelvis may result in bladder and urinary conditions as well as reproductive problems like infertility or loss of libido for men and women. In a report from Georgetown University detailing the recovery of men with prostate cancer who underwent SBRT rates of genitourinary and gastrointestinal toxicity was comparable to standard radio treatment while libido was relatively the same as before therapy [40]. Degen et al. reported that in SBRT treatment of spinal tumors adverse effects were mainly self-limited and included dysphagia, diarrhea, lethargy, and paresthesia [41]. To sum up the occurrences of side effects, it should be well understood that patients undergoing SBRT for cancers can experience a wide range of mostly transient side effects from radiation treatment. The good news is that most of the side effects experienced through SBRT treatment can be reduced with other types of medical intervention making SBRT a safe and effective treatment option for cancerous conditions that would otherwise be fatal.

Limits of SBRT

To date the most apparent limiting factor on whether or not SBRT is indicated as a therapy is the lack of uniform data matching various cancers to treatment plans and radiation dose. In an article on dose tolerance and histogram evaluation of SBRT Grimm et al. stated: "The main obstacle for safe application of the SBRT treatment technique is the unavailability of data that allow unambiguous determination of the parameters for fraction schemes and dose prescriptions" [42]. Also, lifetime radiation limits may play some role in determining which patients are candidates for radiosurgery as opposed to chemotherapy and invasive surgical resection. A secondary limit of SBRT is that due to the precision involved with the procedure, SBRT can only advance as fast as medical imaging technology. As previously stated the latest imaging makes SBRT possible due to the ability to manipulate large doses of radiation in close proximity to vital structures and yet still affect tumor cells. Finally, the scope of cancers that can be treated is broad and presents fewer limitations than the required associated technology. Currently treated cancers are primary and metastatic lung and liver cancers, pancreatic and bile duct cancers, as well as kidney, prostate, pelvic, and spinal column tumors. Further, treatment of

sarcomas, arteriovenous malformations, and trigeminal neuralgia are within scope of SBRT [43].

Conclusion

The authors have attempted to give a brief overview of stereotactic body radiation therapy and its applications. While far from exhaustive the above subject material shows that SBRT is a cutting edge treatment for various cancerous conditions. Use of SBRT for primary, metastatic, benign, and malignant cancers has shown increases in survival rates for all cancers treated with minimal negative side effects. SBRT has also shown to be an effective treatment for patients that have previously undergone surgery, chemotherapy, and radiation and have had cancer relapse. Since SBRT is primarily a non-invasive procedure it is not associated with long recovery times or intensive recovery regimens. The individual SBRT session is relatively quick and the entire treatment program is only days in length. The direct result of a highly effective, noninvasive treatment for cancerous conditions is that in the majority of cases patient lifestyle and overall health are unaffected. Future applications of SBRT will primarily depend on further developments in tumor imaging technology as the delivery of high dose radiation requires a high degree of accuracy and precision.

References

1. <http://www.acr.org/~media/f80a2737ff0f4753b6ababa73e15d757.pdf>.
2. Baldwin DR (2011) Improving outcomes in lung cancer patients. *Practitioner* 255: 19-2.
3. Rajagopalan MS, Heron DE (2010) "Role of PET/CT Imaging in Stereotactic Body Radiotherapy." *Medscape. Medscape.com. Future Oncol.* 6: 305-317.
4. Benedict SH, Yenice KM, Followill D, Galvin JM, Hinson W, et al. (2012) Stereotactic body radiation therapy: the report of AAPM Task Group 101. *Med Phys.* 39: 563.
5. <http://www.lung.org/lung-disease/lung-cancer/resources/facts-figures/lung-cancer-fact-sheet.html>.
6. Zhang H, Das I, Wilson J, Uzan J, Lasley F, et al. (2013) "Evaluation of Tumor Control Probability of Stereotactic Body Radiation Therapy (SBRT) for Primary Liver Cancers." *International Journal of Radiation Oncology Biology Physics* 87.2: S691-S692.
7. Goyal K, Einstein D, Yao M, Kunos C, Barton F, et al. (2010) Cyberknife stereotactic body radiation therapy for nonresectable tumors of the liver: preliminary results. *HPB Surg* 2010: 309780.
8. Grills IS, Mangona VS, Welsh R, Chmielewski G, McInerney E, et al. (2010) Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. *J Clin Oncol* 28: 928-935.
9. Kriminski D, Pavord M, Connor O, Kim A, Farhangi E (2011) SU?E?T? 558: Intrafractional Target Displacement during Stereotactic Body Radiation Therapy in Lung for Patients Immobilized Using BodyFix System *Med. Phys.* 38: 3617.
10. Han K, Cheung P, Basran PS, Poon I, Yeung L, et al. (2010) A comparison of two immobilization systems for stereotactic body radiation therapy of lung tumors. *Radiother Oncol* 95: 103-108.
11. Kruis MF, van de Kamer JB, Sonke JJ, Jansen EP, van Herk M (2013) Registration accuracy and image quality of time averaged mid-position CT scans for liver SBRT. *Radiother Oncol* 109: 404-408.
12. Turzer M, Brustugun OT, Waldeland E, Helland A (2011) Stereotactic body radiation therapy is effective and safe in patients with early-stage non-small cell lung cancer with low performance status and severe comorbidity. *Case Rep Oncol.* 4: 25-34.
13. Zhang Y, Xiao JP, Zhang HZ, Yin WB, Hu YM, et al. (2011) Stereotactic body radiation therapy favors long-term overall survival in patients with lung metastases: five-year experience of a single-institution. *Chin Med J (Engl)* 124: 4132-4137.

14. Matuszak MM, Yan D, Grills I, Martinez A (2010) Clinical applications of volumetric modulated arc therapy. *Int J Radiat Oncol Biol Phys* 77: 608-616.
15. Lee YH, Son SH, Yoon SC, Yu M, Choi BO, et al. (2014) Stereotactic body radiotherapy for prostate cancer: a preliminary report. *Asia Pac J Clin Oncol* 10: e46-53.
16. Chen LN, Suy S, Uhm S, Oermann EK, Ju AW, et al. (2013) Stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer: the Georgetown University experience. *Radiat Oncol* 8:58.
17. <http://radonc.ucla.edu/body.cfm?id=349#indications>.
18. Nikolajek K, Kufeld M, Muacevic A, Wowra B, Niyazi M, et al. (2011) Spinal radiosurgery--efficacy and safety after prior conventional radiotherapy. *Radiat Oncol* 6: 173.
19. Guckenberger M (2011) What is the current status of Stereotactic body radiotherapy for stage I non-small cell lung cancer? *J Thorac Dis* 3: 147-149.
20. Rami EW, Lo SS, Paulino AC, Blanco AI, Butler EB, et al. (2012) "Diagnosis and treatment options including stereotactic body radiation therapy (SBRT) for adrenal metastases." *Journal of Radiation Oncology* 1.1: 43-48.
21. Siva S, Pham D, Gill, S, Corcoran NM, Foroudi F (2012) A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma. *BJU International* 110: E737-E743.
22. Bibault JE, Dewas S, Vautravers-Dewas C, Hollebécque A, Jarraya H, et al. (2013) Stereotactic body radiation therapy for hepatocellular carcinoma: prognostic factors of local control, overall survival, and toxicity. *PLoS One* 8: e77472.
23. Law AL, Ng WT, Lee MC, Chan AT, Fung KH, et al. (2012) Treatment of primary liver cancer using highly-conformal radiotherapy with kV-image guidance and respiratory control. *Radiother Oncol* 102: 56-61.
24. Alongi F, Cozzi L, Arcangeli S, Iftode C, Comito T, et al. (2013) Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study. *Radiat Oncol* 8: 171.
25. Pan HY, Allen PK, Wang XS, Chang EL, Rhines LD, et al. (2014) Incidence and predictive factors of pain flare after spine stereotactic body radiation therapy: secondary analysis of phase 1/2 trials. *Int J Radiat Oncol Biol Phys*. 90: 870-876.
26. <https://www.utoledo.edu/med/depts/radther/pdf/2-22-13%20lecture.pdf>.
27. Edward H, Wazer D, Perez C, Brady L (2013) "Stereotactic Irradiation of Tumors Outside the Central Nervous System." Perez and Brady's *Principals and Practice of Radiation Oncology* (6thedn) Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins.
28. Maria S (2013) "Medscape." Medscape. Medscape.com.
29. Dewas S, Bibault JE, Mirabel X, Fumagalli I, Kramar A, et al. (2012) Prognostic factors affecting local control of hepatic tumors treated by Stereotactic Body Radiation Therapy. *Radiat Oncol* 7:166.
30. Pan H, Simpson DR, Mell LK, Mundt AJ, Lawson JD (2011) A survey of stereotactic body radiotherapy use in the United States. *Cancer* 117: 4566-4572.
31. Senan S, Palma DA, Lagerwaard FJ (2011) Stereotactic ablative radiotherapy for stage I NSCLC: Recent advances and controversies. *J Thorac Dis* 3: 189-196.
32. Masucci GL, Yu E, Ma L, Chang EL, Letourneau D, et al. (2011) Stereotactic body radiotherapy is an effective treatment in reirradiating spinal metastases: current status and practical considerations for safe practice. *Expert Rev Anticancer Ther* 11:1923-1933.
33. Hall WA, Stapleford LJ, Hadjipanayis CG, Curran WJ, Crocker I, et al. (2011) Stereotactic body radiosurgery for spinal metastatic disease: an evidence-based review. *Int J Surg Oncol* 2011: 979214.
34. Baudmann P, Nyman J, Hoyer M, Wennberg B, Gagliardi G, et al. (2009) Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. *J Clin Oncol*. 27: 3290-3296.
35. Katz AW, Carey-Sampson M, Muhs AG, Milano MT, Schell MC, et al. (2007) "Hypofractionated Stereotactic Body Radiation Therapy (SBRT) for Limited Hepatic Metastases." *Science Direct. Int J Radiat Oncol Biol Phys* 67: 793-798.
36. Degen JW, Gagnon GJ, Voyadzis JM, McRae DA, Lunsden M, et al. (2005) CyberKnife stereotactic radiosurgical treatment of spinal tumors for pain control and quality of life. *J Neurosurg Spine* 2: 540-549.
37. Bin ST, Paulino AC, Lu HH, Chiu JK, Richardson S. (2007) "Versatility of the Novalis System to Deliver Image-Guided Stereotactic Body Radiation Therapy (SBRT) for Various Anatomical Sites." *TCRT. Technology in Cancer Research and Treatment* :6.
38. Gill B, Oermann E, Ju A, Suy S, Yu X, et al. (2012) Fiducial-free CyberKnife stereotactic body radiation therapy (SBRT) for single vertebral body metastases: acceptable local control and normal tissue tolerance with 5 fraction approach. *Front Oncol* 2: 39.
39. Chang BW, Saif MW (2008) Stereotactic body radiation therapy (SBRT) in pancreatic cancer: is it ready for prime time? *JOP* 9: 676-682.
40. Dahele M, Fehlings MG, Sahgal A (2011) Stereotactic radiotherapy: an emerging treatment for spinal metastases. *Can J Neurol Sci* 38: 247-250.
41. Waller JG (2013) "Outcomes of Stereotactic Body Radiation Therapy (SBRT) for Hepatocellular Carcinoma (HCC)." *International Journal of Radiation Oncology Biology Physics* 87.2: S326-S327
42. Grimma J, LaCoutureT, Croce R, Yeo I, Zhu Y, et al. (2011) "Dose tolerance limits and dose volume histogram evaluation for stereotactic body radiotherapy". *Journal Of Applied Clinical Medical Physics* 12: 2.
43. Freeman DE, King CR (2011) Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol* 6: 3.