Emerging radiotherapy technology in a developing country: A single Brazilian institution assessment of stereotactic body radiotherapy application

Fabio Ynoe Moraes[1]*, Lorine Arias Bonifacio[1], Wellington Pimenta Neves-Junior[2], Samir Abdallah Hanna[1], Carlos Eduardo Cintra Vita Abreu[1], Fernando Freire Arruda[1], João Luis Fernandes Silva[1], Heloisa Andrade Carvalho[1,3]

[1]Department of Radiation Oncology, Hospital Sírio-Libanês, São Paulo, SP, Brazil
[2]Department of Radiation Oncology and Medical Physics, Hospital Sírio-Libanês, São Paulo, SP, Brazil
[3]Department of Radiology and Oncology, Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil

Summary

Objective: To provide a quantitative profile of the indications and use of stereotactic body radiotherapy (SBRT) in a developing country oncology-based institution. In addition, to describe the patients' and treatment characteristics, and to provide a temporal analysis.

Method: SBRT patients treated from 2007 to 2015 were retrospectively evaluated by two independently investigators. Data were stratified and compared in two periods: first experience (FE) (May 2007 to April 2011), and following experience (FollowE) (May 2011 to April 2015). The following parameters were compared between the groups: total number of treated patients and lesions, treatment site, additional image fusion used, formal protocol adoption, and SBRT planning technique.

Results: One hundred and seventy-six (176) patients with 191 lesions were treated: 34 (18%) lesions in the FE and 157 (82%) lesions in FollowE. The majority of lesions were metastases (60.3%), and lung (60.2%) was the most common treatment site, followed by spine (31%), and others (8.8%). An average of 1.4 (±0.6) additional imaging exams for delineation was performed. Conformal 3D radiotherapy planning technique was used in 64.4%, and intensity modulated radiotherapy (IMRT) or volumetric-modulated arc therapy (VMAT) in the remaining 35.6% (p=0.0001). Higher rates of curative treatments were observed in FE, as well as more lung lesions, patients ≥ 70 years, 3D conformal, number of additional images and ECOG 0, and all presented p<0.05. The global rate of protocol statement was 79%, lung treatment being the most stated.

Conclusion: SBRT application is rapidly increasing in our setting. Treatment sites and planning techniques are becoming more diversified and complex.

Keywords: stereotactic body radiotherapy, radiation oncology, lung neoplasm, radiosurgery.

Study conducted at Hospital Sírio-Libanês, São Paulo, SP, Brazil

Article received: 10/6/2015
Accepted for publication: 11/1/2015

***Correspondence:**
Address: Rua Dona Adma Jafet, 91
São Paulo, SP – Brazil
Postal code: 01308-050
fymoraes@gmail.com

http://dx.doi.org/10.1590/1806-9282.62.08.782

Introduction

In 2008, a global survey of cancer epidemiology revealed that about 12.7 million cancer cases and 7.6 million cancer deaths were estimated to occur worldwide, with 56% of the cases and 64% of the deaths in the economically developing world.[1] Data from the World Health Organization (WHO) estimated in 2012 about 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer (within 5 years of diagnosis) worldwide,[2] showing a rising pattern and a tendency towards a longer life period with cancer diagnosis. This may reflect the improvements on screening, diagnosis, surgery, chemotherapy, radiation therapy, and other anti-cancer modalities.

Regarding radiation oncology, technological advances are continuously providing more effective and safe treatments. Intracranial lesions have been successfully treated with stereotactic radiosurgery (SRS) for years, due

to the precise delivery of a high dose of radiation to the tumor bed, with very low doses to the surrounding critical tissues.[3] These results have encouraged the development of stereotactic body radiotherapy (SBRT), which could be implemented due to the advances in image-guided radiotherapy procedures.

SBRT, or stereotactic ablative radiotherapy (SABR), is a technique developed to deliver high and ablative doses of radiation either in one or up to five fractions in primary or oligometastatic disease, mainly in lung, liver, and spine, with very low rates of moderate to high-grade toxicity. Although started in the early 1990's, only recently it has been receiving more attention for being a minimally invasive technique with high effectiveness and patient convenience.[4]

Primary SBRT goals are to achieve better local control, delay progression, postpone the need of further treatment, improve quality of life, and even impact the overall survival. Emerging evidence suggests that despite site and histology, local control rates for metastasis (especially lung, spine, and liver) treated with SBRT are roughly 80% and more.[5]

The possibility of delivering radiation in a single high dose or within short radiation courses of high doses per fraction is very attractive. SBRT application for curative or palliative purposes is becoming more popular, even though the technology for such treatments is not often available worldwide. Despite great background and clinical outcomes, little is known about use and prevalence of SBRT, especially in low income and Latin American countries; however, efforts are being made to change this scenario.[6,7] Previous surveys were conducted in the USA and Japan.[8,9] To our knowledge, this article is the first representation of the SBRT profile, its application and temporal trends from a Latin American institution, which can add knowledge to the literature and may be used as a benchmark for future wider analysis.

The aim of this study was to provide a quantitative profile of the indications and use of SBRT in a developing country oncology-based institution. In addition, we sought to describe the patients' and treatment characteristics, and to provide a temporal analysis of the experience using the SBRT technique. We also aimed to compare two distinct periods, report the learning curve for the use of SBRT and procedure diversification.

Method

Data from consecutive patients treated from May 2007 (first treated patient) to April 2015 were retrospectively collected from medical charts and system planning information. All patients treated using the SBRT technique were included in the analysis. SBRT was defined as treatments with prescribed doses per fraction equal or higher than 8 Gy, delivered in 1 to 5 fractions (Lung $BED_{Gy10} \geq 70$ Gy; Spine $BED_{Gy3} \geq 75$ Gy; Liver $BED_{Gy3} \geq 145$ Gy).

The two independent investigators (F.Y.M. and L.A.B.) extracted demographics data (such as age, sex, tumor location, stage, and performance status). Technical and dosimetric data were also assessed and included: treatment site, fractionation, total treatment dose, planning technique (three-dimensional conformal radiotherapy – 3DCRT, intensity modulated radiotherapy – IMRT, and volumetric-modulated arc therapy – VMAT), additional images were used for target delineation, protocol or guideline followed for treatment, and period of treatment. Missing data was doubled checked on chart and planning system software. For the descriptive analysis, no data were missing after double checks as the planning system data was very accurate (we perform at our institution a double check on clinical and technical information on every treatment before their start, which may explain the quality of charts).

A descriptive analysis was performed for patients and technical characteristics. A subgroup descriptive analysis was also performed, dividing the sample in two groups, based on the period of treatment: from May 2007 to end of April 2011 [first 47 months of SBRT use or our first experience (FE)] and from May 2011 to April 2015 [47 following months of SBRT use or following experience (FollowE)]. Thus, each group comprises 47 months of the institution's experience in performing SBRT. From now on, these groups will be referred to respectively, as "FE" and "FollowE." With this comparison, we aimed to show a learning curve, and the more diversified sites of SBRT treatment, not that a period was better than the other.

The following parameters were compared between the groups: total number of treated patients and lesions, treatment site, additional image fusion used, formal protocol adoption, and SBRT planning technique. A comparison between the number of SBRTs performed along the years and sites of treatment is presented. A comparison between the numbers of published papers related to the topic over the same period in the Pubmed database (Mesh terms: "Radiosurgery," "no language restrictions," "from 2007 to 2015") was also performed and presented in the discussion.

Statistical considerations

Descriptive data are presented as percentage of evaluable data. Central tendency and dispersion measures were used to summarize numeric variables. Differences in percentages between FE and FollowE groups were analyzed using

chi-square tests (with Fisher corrections). Statistically significant levels were set at p≤0.05.

Results

In our study, 176 consecutives patients were included accounting for 191 treated lesions. Male (65.3%) was the most common gender. Median age was 66.9 years (standard deviation ±14,4) and ECOG performance status was 0 in 69/176 (36%) of the patients, 1 in 45%, 2 in 11%, and 3 in only 2.8% (5.2% of the patients had no register of the performance status, and could not be classified). The majority of the cases were treated due to metastasis (60.3%) and the others, primary tumors (39.7%). The most frequent treatment site (curative and/or palliative intention) was lung (60.2%), followed by spine or bone (30.8%), liver, prostate, and others. One patient had more than one site treated: lung and bone. Among the 39.7% (76/191 lesions) treatments with curative intention, lung cancer was the main indication (88.1%, 67/76 curative treatments) followed by spine or bone (6/76), and others (3/76). On palliative setting, spine or bone was the main treated site (46%, 53/115 palliative treatment) followed by lung metastases (48/115) and others (14/115).

The correspondent treatment characteristics of the two studied periods (FE – May 2007 to April 2011, and FollowE – May 2011 to April 2015) was: (1) at FE, lung prevailing (79.4%, 27/34 treatments) over spine (6/34) and others (1/34); and at (2) FollowE, lung lesion still prevailing (56%, 88/157 treatments) over spine or bone (53/157) and others (16/157).

In FE, higher rates of curative treatment (OR 2.09, p=0.0005), lung lesions (OR 3.85, p=0.0198), patients ≥ 70 years (OR 2.77, p=0.0005), 3D conformal planning (OR 16, p=0.0001), lower number of additional images (0 or 1 *vs.* > 1) (OR 7.5, p=0.0001) and ECOG 0 (versus > 0) (OR 0.21, p=0.0431) were observed. Summary of SBRT treatments performed in 176 patients are presented in Table 1.

The additional imaging exams used for delineation of gross tumor volume (GTV) and surrounding normal tissues are presented in Figure 1. A median of one (range 1 to 3) additional exam was performed in 94.2% of all 191 treated lesions, mostly in the FollowE (Table 1). The median time between the day of treatment simulation and the beginning of treatment was 11 days (range 2 to 28 days). The median number of fractions prescribed was three (range 1 to 5 fractions), with single fraction representing 22.2%, 2-fractions 0.6%, 3-fractions 46.8%, 4-fractions 1.5% and 5-fractions 28.9%. The median dose per fraction was 15 Gy (range 8 to 26 Gy) and the median total dose was 45 Gy (range 14 to 60 Gy). The most common fractionation schedules were 16 Gy and 18 Gy for one fraction (respectively 11 and 13 of 42 lesions), 15 Gy and 18 Gy for three fractions (31 and 35 of 89 lesions, respectively), and, for five fractions, 8 Gy (13/55) and 10 Gy (19/55), respectively. The planning and delivery techniques used are presented in Figure 2.

The majority of formal protocol reports were related to lung treatments (83.4%, 96/115 lung lesions treatments) followed by spine treatments (39/59) and others (8/17). The global rate of protocol statement was 79%.

Discussion

Considerable improvements in radiotherapy (RT) approach, planning and delivery techniques are reflecting in treatment demographics. Over the studied period, 191 lesions in 176 patients were treated with SBRT at our

TABLE 1 Summary of SBRT treatments performed in 176 patients (191 lesions) from May 2007 to April 2011 (first experience), and from May 2011 to April 2015 (following experience). Percentages of treatment characteristics are related to the number of treated lesions.

		First 47 months	Following 47 months	Total	P
Number of patients		34	142	176 (100%)	**0.0198**
Number of lesions treated		34 (17.8%)	157 (82.2%)	191 (100%)	
Site	Lung	27 (79.5%)	88 (56.1%)	115 (60.2%)	
	Spine	6 (17.6%)	53 (33.7%)	59 (31%)	
	Others	1 (2.9%)	16 (10.2%)	17 (8.8%)	
Total additional images used for delineation		30/262 (11.4%)	232/262 (88.6%)		**0.0001**
Statement of protocol adoption		21/34 (61.7%)	121/157 (77.7%)	142/191 (74.3%)	0.0822
Treatment planning technique	3DCRT	32 (94.1%)	91 (58.0%)	123 (64.4%)	**0.0001**
	IMRT or VMAT	2 (5.9%)	66 (42%)	68 (35.6%)	

3DCRT: three-dimensional conformal radiotherapy; IMRT: intensity modulated radiotherapy; VMAT: volumetric-modulated arc therapy.

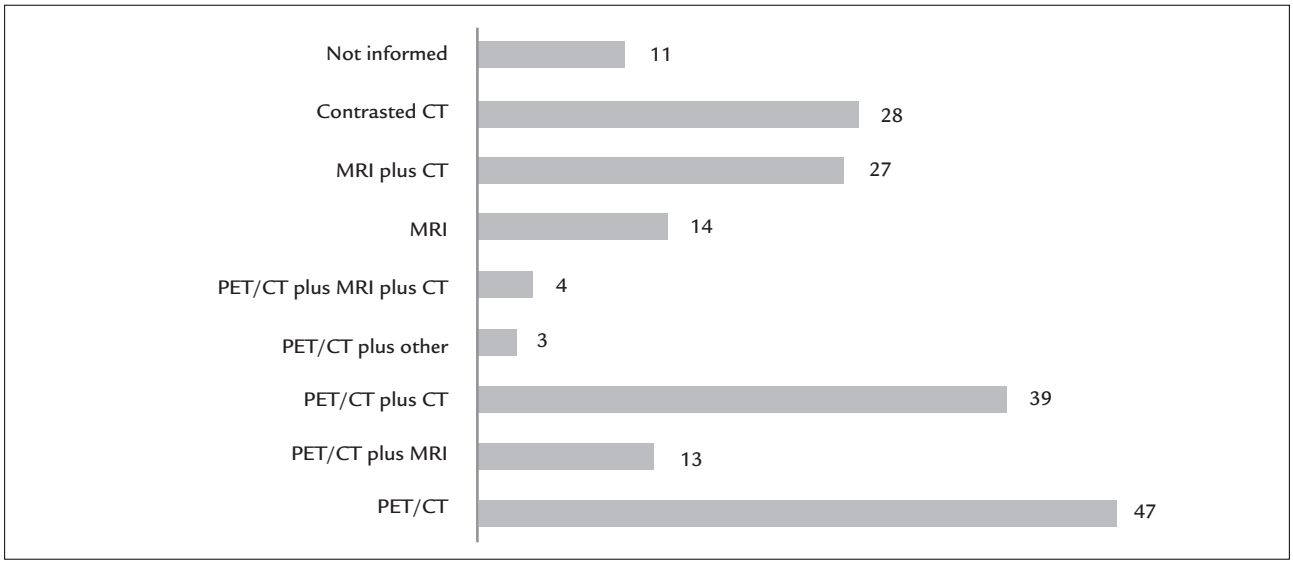

FIGURE 1 Additional images used for tumor/normal tissue delineation. Many patients had more than one additional exam for volume delineation.
CT: computed tomography; MRI: magnetic resonance imaging; PET: positron emission tomography.

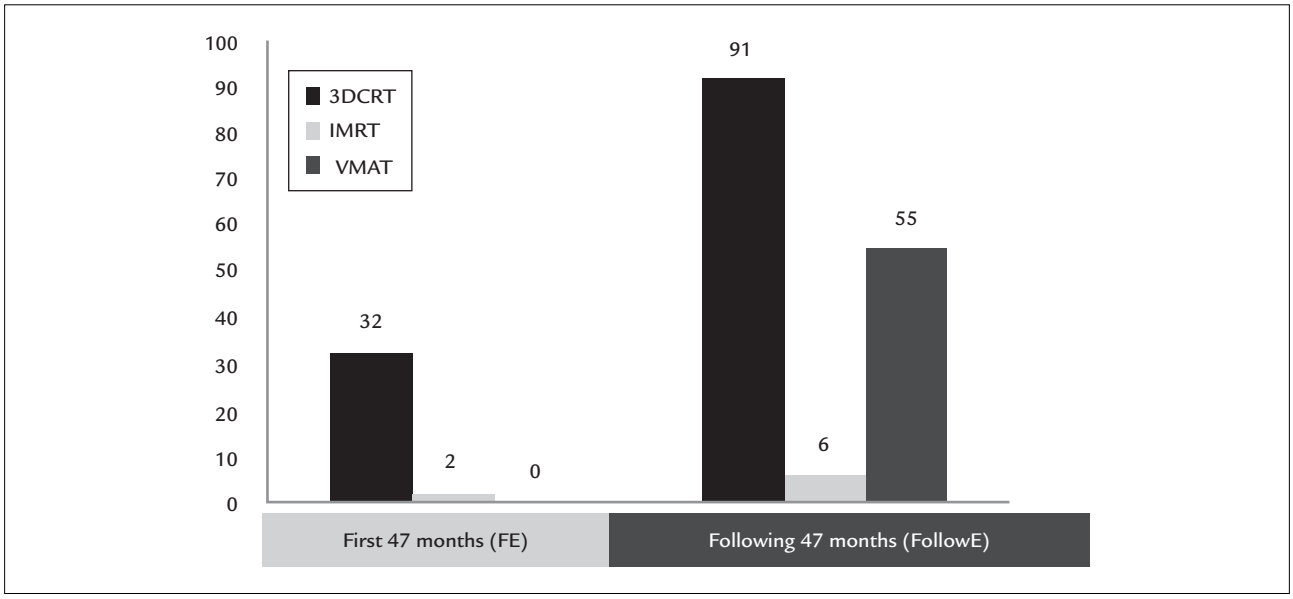

FIGURE 2 Treatment planning techniques per period.
VMAT: volumetric-modulated arc therapy; 3DCRT: three-dimensional conformal radiotherapy; IMRT: intensity modulated radiotherapy; FE: first experience; FollowE: following experience.

institution. Overall, the population was elderly, with metastatic disease (60.3%), but most presented good performance status (81% ECOG 0 or 1), and most were treated with three or five fractions of SBRT.

These results emphasize the choice of SBRT, in our institution, for patients with good performance status even with metastatic disease in agreement with the fact that SBRT is an interesting option for patients with oligometastatic disease, that have good life expectancy. Curative treatment was indicated in 39.7% of the cohort, mostly for lung cancer. This finding is consistent with the availability of a wide literature that discusses the local control and long-term survival outcomes of SBRT for stage I non-small cell lung cancer, suggesting that comparable results to surgical approach can be achieved.[5]

We observed an important increase in SBRT procedures from the FE (17.8%) to the FollowE period (82.2% of 191 lesions). In the 12-month period of this analysis

(from January 2013 to February 2014), the department performed 969 radiotherapy treatment plans (3D-conformal or more complex), so that 458 (47.3%) comprised IMRT (step-and-shoot), VMAT, cranial radiosurgery, and SBRT. In this 12-month period, SBRT corresponded to 6% of all plans and 13% of the complex planning (out of 59 treatments planning), showing the impact of SBRT planning in our routine.

When looking for peer reviewed published articles regarding SBRT (all sites) on Pubmed database (MeSh terms: "Radiosurgery," "no language restrictions," "from 2007 to 2015") there was a significant absolute increase of papers. From the 5,365 papers retrieved, 1,985 (37%) were published in the FE and 3,380 (63%) in the FollowE period. Increase of publication is also reported for many other techniques and sub sites, such as central nervous system neoplasms.[10] The spread of the results of application of more complex technologies in the clinical setting provides better support for SBRT application, which might explain the increasing indication of the technique in our institution. Together with the favorable data from the literature, the expected learning curve may also explain the raise in SBRT indications along the years.

This also may explain the diversity in the indication of treatment sites and planning techniques over time, reflecting more confidence to perform SBRT. In addition, more imaging exams were used for tumor location and delineation in the FollowE. This could even be due to the availability of more exams in the institution, as well as more detailed publications and/or recommendations on the subject, and the potential to achieve a lower toxicity more accurately.

In our data, lung was by far the main treated site along the years. This might be related to the disease prevalence, as well as with the wide and well-established literature of SBRT for pulmonary lesions.[11,12] The second most treated site was spine, which has low/moderate level of evidence publications and some available protocols.[13,14] Prostate and liver neoplasms were less frequent; however, there are also many studies reporting the use of SBRT in these sites and feasible protocols available.[15,16]

Although our results have shown 25.7% of treatments without a formal protocol statement, a protocol was indeed followed, even though not reported, respecting the dose constraints in healthy surrounding tissue and planning report, in the treatment of all patients. This is in accordance with the institutional policy. Lung neoplasms were treated regarding to tumor location (central and peripheral lesion) and mainly two Radiation Therapy Oncology Group (RTOG) protocols were followed – RTOG 0236 and RTOG 0813.[14,17] Spinal metastatic lesions half of the times were formally managed according to the RTOG 0631 protocol and target definition was mostly based on an international consensus.[13,18] This illustrates the positive impact that international protocols and recommendations have in our setting.[20-24]

An USA national survey from 510 radiation oncologists in 2010 reported that lung followed by spine and liver were the most common sites of SBRT treatment and three fractions were the most common fractionation used. They also reported a fast increase on SBRT application (from less than 10% in 2000 to 65% in 2010) and most of the centers are planning to increase the SBRT applications. It is important to notice that the majority of respondents who were using SBRT started between 2007 and 2008 and, to the date of the survey, 63.9% of the analyzed centers were adopting SBRT treatments.[9]

A Japanese nationwide survey conducted by the end of 2005 reported that lung cancer, followed by liver (primary and metastatic tumors), was the most common site of SBRT treatment. They reported that the average number of involved radiation oncologists was 1.8 per treatment and that treatment planning was the most consuming time (60 to 120 minutes), followed by quality assurance (QA) (50 to 60 min) and daily treatment delivery (< 60 min).[10]

Also, a Canadian survey reported 14 centers over 41 performing SBRT. Only 11 completed the full survey and the most common sites of treatment per center were lung (13/14 center), liver (9/14 center), and spine (5/14 center). They also reported a broad range of image guidance, use of fiducials, and strategies to minimize tumor movement. Interestingly, the record showed that 18% of the centers performed routine peer review of targets volumes and planning for all sites treated with SBRT.[19]

Since SBRT is a relatively new technique which requires a high technology, not surprisingly, most of the patients (63.5%) were submitted to PET-CT in our series and had their lesions diagnosed/followed by this exam. This finding should be considered with care since, at least in our country, this is an expensive procedure available only in a few selected medical centers.

The median time from simulation to treatment was 11 days, even though it was possible to treat a patient in 48 hours. SBRT is a complex procedure that, besides a precise medical simulation/planning, requires a thorough quality control performed by the medical physics team. The longest period of delay (28 days) was due to an unexpected patient event, and longer delays were related to patients that had more than one lesion to be treated.

The most adopted technique was 3DCRT (64.4%), always planned with more than 10 non-coplanar beams arrangement. The rational of the institution is to always apply the simplest delivery method possible on each case. Thus, 3DCRT is the preferred delivery method for simpler cases (i.e. no critical organs nearby) and, specially, when the target moves (less dose blurring and leaf motion interplay effects compared to intensity modulated techniques). Therefore, 3DCRT is the preferred choice for the majority of lung (RTOG protocols 0236 and 0813 do not recommend highly modulated fields)[14,23] and liver cases. IMRT was used in few situations and was rapidly substituted by VMAT as soon as this technology turned available in the institution, due to the shorter treatment time and more comfort for the patients.

Currently, intensity modulated techniques are reserved to cases where a high gradient is needed to spare a near critical organ, such as in all spine cases, selected centrally located lung lesions and more complex liver cases. All lung and liver cases included in this study were planned with individualized internal target volumes (ITV) created through motion studies performed with three CT series technique (deep inspiration/expiration and free breathing) – which was replaced nowadays by four-dimensional CT (4DCT) simulation. No further motion management or ITV reduction technique was applied (such as abdominal compression or gating). Patient positioning was always performed with cone beam CT image guidance (either kV or MV) and, for a portion of spinal cases, X-rays image guidance was combined.

The retrospective design and time-limited single institution analysis could be seen as limitations of the current study. However, it provides information regarding SBRT application outside the developed world, protocol/guidelines applications on clinical setting, use of additional images for GTV delineation, and improvements on planning techniques along time. In addition, it provides original data on the rise of new technology applications of radiotherapy and can influence new emerging centers to implement and perform SBRT (the most common reported reasons for not performing SBRT were lack of clinical expertise and the necessary technology). Data from non-performing SBRT centers from Canada show that 50% intend to start within 1-year and 70% within 5 years, and this may be a reality in other countries.[25]

Conclusion

In our setting, clinical application of SBRT increased and became more diversified along time. Planning techniques are becoming more complex and can improve equipment capacity and enhance patient convenience. Palliative approach and patient with good performance status were predominant for SBRT application.

Resumo

Tecnologias emergentes em radioterapia em um país em desenvolvimento: perfil do uso de radiocirurgia extracraniana em uma instituição filantrópica privada

Objetivo: realizar uma análise quantitativa das indicações e do uso de SBRT (*stereotactic body radiotherapy*) em uma instituição filantrópica. Além disso, descrever temporalmente as características dos pacientes e tratamentos.
Método: retrospectivamente, foram coletados, por dois investigadores independentes, os dados de todos os pacientes tratados com SBRT na instituição no período de maio de 2007 a fevereiro de 2015. Dados foram estratificados e comparados em dois períodos: inicial (P1) (maio de 2007 a abril de 2011) e período seguinte (P2) (maio de 2011 a abril de 2015). Os seguintes parâmetros foram comparados entre os grupos: número total de pacientes e lesões tratadas, local de tratamento, uso de imagens adicionais, adoção formal de protocolo e técnica de planejamento.
Resultados: foram avaliados 176 pacientes e 191 lesões, sendo 34 (18%) no P1 e 157 (82%) no P2, tratados com SBRT. A maioria das lesões eram metastáticas (60,3%), sendo pulmão o sítio mais prevalente, contabilizando 115/191 (60,2%) lesões, seguida de lesões ósseas (30,8%). Uma média de 1,4 (±0,6) exame de imagem adicional foi usada para o delineamento. Uso formal de protocolo/recomendações foi descrito em 79% das lesões. A técnica 3D-conformada (3DCRT – *three-dimensional conformal radiotherapy*) foi a mais utilizada para planejamento [123/191 (64,4%) lesões] quando comparada à intensidade modulada e ao arco dinâmico (p=0.0001). O P1 esteve associado a maior número de lesões primárias tratadas (OR 2,09; p=0,0005), lesões pulmonares (OR 3,85; p=0,0198), pacientes ≥ 70 anos (OR 2,77; p=0,0005), uso de planejamento 3D (OR 16; p=0,0001), menor uso de imagens adicionais [0 ou 1 (*versus* > 1)] (OR 7,5; p=0,0001) e ECOG 0 (*vs.* > 0) (OR 0,21; p=0,0431).
Conclusão: o uso de SBRT aumentou ao longo do tempo na instituição. No P2, notou-se uma evolução técnica, com indicações mais diferenciadas, maior uso de imagens auxiliares para definição do alvo e técnicas de planejamento mais sofisticadas.

Palavras-chave: radioterapia estereotáxica extracraniana, radio-oncologia, neoplasia de pulmão, radiocirurgia.

References

1. Videtic GMM. The development of stereotactic body radiotherapy (SBRT) for medically inoperable early stage non-small cell lung cancer: an international phenomenon. J Radiat Oncol. 2012; 1(1):3-10.
2. WHO. Globocan 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. [cited 2014 Mar 5]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.
3. Rubio C, Morera R, Hernando O, Leroy T, Lartigau SE. Extracranial stereotactic body radiotherapy. Review of main SBRT features and indications in primary tumors. Rep Pract Oncol Radiother. 2013; 18(6):387-96.
4. Kavanagh BD, McGarry RC, Timmerman RD. Extracranial radiosurgery (stereotactic body radiation therapy) for oligometastases. Semin Radiat Oncol. 2006; 16(2):77-84.
5. Tree AC, Khoo VS, Eeles RA, Ahmed M, Dearnaley DP, Hawkins MA, et al. Stereotactic body radiotherapy for oligometastases. Lancet Oncol. 2013; 14(1):e28-37.
6. Atun R, Jaffray DA, Barton MB, Bray F, Baumann M, Vikram B, et al. Expanding global access to radiotherapy. Lancet Oncol. 2015; 16(10):1153-86.
7. Rodin D, Jaffray D, Atun R, Knaul FM, Gospodarowicz M; Global Task Force on Radiotherapy for Cancer Control and the Union for International Cancer Control. The need to expand global access to radiotherapy. Lancet Oncol. 2014; 15(4):378-80.
8. Moraes FY de, Marta GN, Hanna SA, Leite ETT, Ferrigno R, da Silva JLF, et al. Brazil's Challenges and Opportunities. Int J Radiat Oncol Biol Phys. 2015; 92(4):707-12.
9. Pan H, Simpson DR, Mell LK, Mundt AJ, Lawson JD. A survey of stereotactic body radiotherapy use in the United States. Cancer. 2011; 117(19):4566-72.
10. Nagata Y, Hiraoka M, Mizowaki T, Narita Y, Matsuo Y, Norihisa Y, et al. Survey of stereotactic body radiation therapy in Japan by the Japan 3-D Conformal External Beam Radiotherapy Group. Int J Radiat Oncol Biol Phys. 2009; 75(2):343-7.
11. Moraes FY, Bonifacio LA, Marta GN, Hanna SA, Atallah AN, Moraes VY, et al. Hierarchy of evidence referring to the central nervous system in a high-impact radiation oncology journal: a 10-year assessment. Descriptive critical appraisal study. Sao Paulo Med J. 2015; 133(4):307-13.
12. Senthi S, Haasbeek CJA, Slotman BJ, Senan S. Outcomes of stereotactic ablative radiotherapy for central lung tumours: a systematic review. Radiother Oncol. 2013; 106(3):276-82.
13. Chang JY, Liu Y-H, Zhu Z, Welsh JW, Gomez DR, Komaki R, et al. Stereotactic ablative radiotherapy: a potentially curable approach to early stage multiple primary lung cancer. Cancer. 2013; 119(18):3402-10.
14. Timmerman RD, Hu C, Michalski J, Straube W, Galvin J, Johnstone D, et al. Long-term results of RTOG 0236: a phase II trial of stereotactic body radiation therapy (SBRT) in the treatment of patients with medically inoperable stage I non-small cell lung cancer. Int J Radiat Oncol Biol Phys. 2014; 90(1):S30.
15. Ryu S, Pugh SL, Gerszten PC, Yin FF, Timmerman RD, Hitchcock YJ, et al. RTOG 0631 phase 2/3 study of image guided stereotactic radiosurgery for localized (1-3) spine metastases: phase 2 results. Pract Radiat Oncol. 2014; 4(2):76-81.
16. Laufer I, Rubin DG, Lis E, Cox BW, Stubblefield MD, Yamada Y, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. Oncologist. 2013; 18(6):744-51.
17. Yamada Y, Lovelock M, Bilsky M, Zatcky J, Hunt M, Fuks Z. Single fraction image guided intensity modulated radiation therapy (IG IMRT) for metastatic lesions of the spinal column. Int J Radiat Oncol Biol Phys. 2005; 63(Suppl 1):S155.
18. Moraes FY, Siqueira GMS, Abreu CECV, da Silva JLF, Gadia R. Hypofractioned radiotherapy in prostate cancer: is it the next step? Expert Rev Anticancer Ther. 2014; 14(11):1271-6.
19. King CR, Brooks JD, Gill H, Pawlicki T, Cotrutz C, Presti JC Jr. Stereotactic body radiotherapy for localized prostate cancer: interim results of a prospective phase II clinical trial. Int J Radiat Oncol Biol Phys. 2009; 73(4):1043-8.
20. McBride SM, Wong DS, Dombrowski JJ, Harkins B, Tapella P, Hanscom HN, et al. Hypofractionated stereotactic body radiotherapy in low-risk prostate adenocarcinoma: preliminary results of a multi-institutional phase 1 feasibility trial. Cancer. 2012; 118(15):3681-90.
21. Herfarth KK, Debus J, Lohr F, Bahner ML, Rhein B, Fritz P, et al. Stereotactic single-dose radiation therapy of liver tumors: results of a phase I/II trial. J Clin Oncol. 2001; 19(1):164-70.
22. Soliman H, Ringash J, Jiang H, Singh K, Kim J, Dinniwell R, et al. Phase II trial of palliative radiotherapy for hepatocellular carcinoma and liver metastases. J Clin Oncol. 2013; 31(31):3980-6.
23. Bezjak A. Seamless phase I/II study of stereotactic lung radiotherapy (SBRT) for early stage, centrally located, non-small cell lung cancer (NSCLC) in medically inoperable patients, Protocol 0813. Philadelphia: RTOG, 2009. [cited 2014 Sep 25]. Available from: http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0813.
24. Cox BW, Spratt DE, Lovelock M, Bilsky MH, Lis E, Ryu S, et al. International Spine Radiosurgery Consortium consensus guidelines for target volume definition in spinal stereotactic radiosurgery. Int J Radiat Oncol Biol Phys. 2012; 83(5):e597-605.
25. Lund CR, Ma R, Carolan H, Liu M, Schellenber D. The current patterns of practice for stereotactic body radiotherapy in Canada. Int J Radiat Oncol Biol Phys. 2011; 81(2 Suppl):S559.