Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 3, pp. 1278–1284, 2012

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2011.02.005

CLINICAL INVESTIGATION **Central Nervous System**

VOLUMETRIC MODULATED ARC–BASED HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR THE TREATMENT OF SELECTED INTRACRANIAL ARTERIOVENOUS MALFORMATIONS: DOSIMETRIC REPORT AND EARLY CLINICAL EXPERIENCE

Sai Subramanian, M.Sc.,* Chilukuri Srinivas, M.D.,* K. Ramalingam, M.Sc.,* M. Babaiah, M.D.,* S. Thirumalai Swamy, M.Sc.,* G. Arun, M.Sc.,* M. Kathirvel, M.Sc.,* S. Ashok, M.Sc.,* Alessandro Clivio, M.Sc.,† Antonella Fogliata, M.Sc.,† Giorgia Nicolini, M.Sc.,† K. Srinivasa Rao, M.D.,* T. Pratap Reddy, M.D.,* Jotwani Amit, M.D.,* Eugenio Vanetti, M.Sc.,† and Luca Cozzi, Ph.D.†

*Yashoda Super Specialty Hospital, Hyderabad, India; and †Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Purpose: To evaluate, with a dosimetric and clinical feasibility study, RapidArc (a volumetric modulated arc technique) for hypofractionated stereotactic radiotherapy treatment of large arteriovenous malformations (AVMs).
Methods and Materials: Nine patients were subject to multimodality imaging (magnetic resonance, computed tomography, and digital subtraction angiography) to determine nidus and target volumes, as well as involved organs at risk (optical structures, inner ear, brain stem). Plans for multiple intensity-modulated arcs with a single isocenter were optimized for a fractionation of 25 Gy in 5 fractions. All plans were optimized for 6-MV photon beams. Dose–volume histograms were analyzed to assess plan quality. Delivery parameters were reported to appraise technical features of RapidArc, and pretreatment quality assurance measurements were carried out to report on quality of delivery.
Results: Average size of AVM nidus was 26.2 cm^3, and RapidArc plans provided complete target coverage with minimal overdosage ($V_{100\%}$ = 100% and $V_{110\%}$ < 1%) and excellent homogeneity (<6%). Organs at risk were highly spared. The $D_{1\%}$ to chiasm, eyes, lenses, optic nerves, and brainstem (mean ± SD) was 6.4 ± 8.3, 1.9 ± 3.8, 2.3 ± 2.2, 0.7 ± 0.9, 4.4 ± 7.2, 12.2 ± 9.6 Gy, respectively. Conformity index ($CI_{95\%}$) was 2.2 ± 0.1. The number of monitor units per gray was 277 ± 45, total beam-on time was 2.5 ± 0.3 min. Planning vs. delivery γ pass rate was 98.3% ± 0.9%. None of the patients developed acute toxicity. With a median follow-up of 9 months, 3 patients presented with deterioration of symptoms and were found to have postradiation changes but responded symptomatically to steroids. These patients continue to do well on follow-up. One patient developed headache and seizures, which was attributed to intracranial bleed, confirmed on imaging.
Conclusion: Hypofractionated stereotactic radiotherapy can be successfully delivered using the RapidArc form of volumetric arc technology for intracranial AVMs. The quality of delivery and calculated parameters are in agreement with each other and are in line with published reports for other sites.

Arterovenous malformation, RapidArc, Volumetric modulated arc therapy, Stereotactic radiotherapy.

INTRODUCTION

Single-fraction stereotactic radiosurgery has been an acceptable treatment for intracranial arteriovenous malformations (AVMs) (1–8). The aim of treatment is to achieve complete obliteration while limiting postradiosurgery sequelae to a minimum. Success of the treatment depends on appropriate patient selection and the marginal dose delivered. However, in large AVMs and in AVMs located in eloquent areas like the sensorimotor cortex, visual cortex, internal capsule, deep cerebellar nuclei, brainstem, thalamus, and hypothalamus, the probability of long-term sequelae is high. Flickinger *et al.* (9) developed a model to predict postradiosurgery symptomatic sequelae on the basis of location and volume of brain receiving medium–high dose levels (9).

Because in such AVMs surgery is not feasible and neuroradiologic interventions are singularly not effective,

Reprint requests to: Antonella Fogliata, M.Sc., Oncology Institute of Southern Switzerland, Radiation Oncology Department, Medical Physics Unit, 6504 Bellinzona, Switzerland. Tel: (+41) 91-8119202; Fax: (+41) 91-8118678; E-mail: antonella.fogliata-cozzi@eoc.ch

Conflict of interest: L.C. acts as Scientific Advisor to Varian Medical Systems and is Head of Research and Technological Development at the Oncology Institute of Southern Switzerland, Bellinzona.

Received Oct 13, 2010, and in revised form Jan 26, 2011. Accepted for publication Feb 3, 2011.

hypofractionated stereotactic radiotherapy (HSRT) has been evaluated for the treatment of large AVMs and those located in eloquent areas (1, 5–7, 10–14). This technique combines the physical advantage of stereotaxy and the radiobiologic advantage of fractionation. The fractionation would be beneficial if the α/β ratio of the AVM nidus is relatively higher than the α/β ratio of adjacent normal brain tissue. Traditionally, various fractionation schemes (25–36 Gy/5–8 fractions) have been used and have been found effective (1, 15–17).

Conventionally, these treatments have been given with dynamic conformal arcs (2, 4–7, 11–14), and recently intensity-modulated stereotactic treatments have been introduced (3, 10). Advanced techniques as treatment with robot-driven linear accelerators were investigated as well, with reports on early clinical experiences (18, 19).

In this study we evaluated volumetric modulated arc therapy (VMAT) for the treatment of these lesions with HSRT.

Volumetric modulated arc therapy, based on the original investigation of Otto (20), has been recently introduced in clinical practice in several institutes after an intensive validation at the planning level, compared with intensity-modulated radiotherapy (IMRT) or other approaches. RapidArc, the Varian Medical Systems (Palo Alto, CA) solution of VMAT, is implemented as the Progressive Resolution Optimization algorithm in the Eclipse planning system (Varian Medical Systems). The optimization process is based on an iterative inverse planning process aiming to simultaneously optimize the instantaneous multileaf collimator (MLC) positions, dose rate, and gantry rotation speed to achieve the desired dose distribution.

Preclinical validation of RapidArc was addressed in a series of studies including brain tumors, head and neck, anal canal, cervix uteri cancer, and other indications (21–26). Stereotactic application of RapidArc was investigated for brain, spinal cord, abdominal, and lung tumors (27–31).

Early clinical reports appeared for prostate, rectal, head-and-neck, and brain tumors (28–34). In all cases, data published suggested technical feasibility of VMAT-based IMRT with RapidArc and an absence of unexpected acute side effects or complications. Clinical long-term results are still awaited owing to inadequate follow-up time because this technology was introduced only recently.

The aim of the present study was to report the clinical feasibility as well as the technical and dosimetric aspects of treatment of AVMs with RapidArc.

METHODS AND MATERIALS

Nine consecutive patients qualifying for hypofractionated treatments based on institutional protocol were included in the study. A team of neurosurgeons, radiation oncologists, neuroradiologists, and interventional radiologists carried out an initial assessment based on results of digital subtraction angiography (DSA) and computed tomography (CT) or magnetic resonance angiography (MRA). Our institutional policy for the treatment of AVMs is outlined in Fig. 1. The policy for treatment of small AVMs (<3 cm nidus) located in noneloquent areas depends on patient characteristics

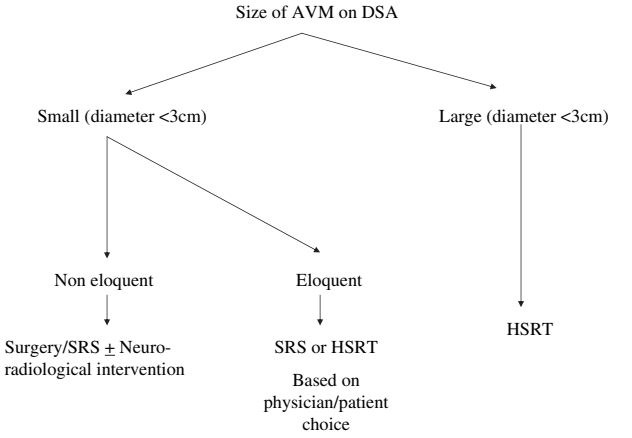

Fig. 1. Flow chart of the institutional policy for treatment of arteriovenous malformations (AVM). Treatment selection is performed according to arteriovenous malformation size at digital subtraction angiography (DSA). Surgery is considered only for smaller lesions in noneloquent regions. SRS = stereotactic radiosurgery; HSRT = hypofractionated stereotactic radiotherapy.

and surgeon preference. The AVMs were classified according to the Spetzler–Martin grading system (35). All large AVMs presented in this study were treated with HSRT to a total dose of 25 Gy in 5 fractions. Patient characteristics and descriptive information on pathology are summarized in Table 1. The follow-up protocol consists of MRA and neuro-ophthalmic assessment at 6 weeks, 6 months, and yearly thereafter. In case of complete obliteration on MRA, the findings are confirmed on DSA.

After informed consent from and detailed discussion with the patients, the treatment workup included various imaging sessions. A planning MR scan was performed with a three-dimensional (3D) fast spoiled gradient recovery sequence in which axial postcontrast MR sections were obtained with 1.5-mm slice thickness and no interslice gap at equal-size matrix (256 × 256). A DSA was done through the femoral artery route, with the stereotactic mask and localizer box in place. A planning CT scan with contrast was also obtained in the same position.

All three imaging sequences were transferred to the Eclipse treatment planning system and were fused for delineation of target and organs at risk. The nidus with feeding vessels in filling phase was identified on the DSA and was marked as target (gross target volume). A margin of 5 mm was added to generate the planning target volume (PTV). Organs at risk, such as optic chiasm, optic nerves, pituitary–hypothalamic axis, brainstem, internal ears, bilateral retina, lenses, and normal brain were delineated.

Contoured images were then localized for SRT coordinates in the iPlan system (version 4.1.1; BrainLab, Feldkirchen, Germany) after Digital Imaging and Communications in Medicine–based data transfer between the systems. The isocenter was positioned in the center of the target volume and data sent back to Eclipse for planning. Target positioning printouts were generated from iPlan, and patients were aligned on the treatment couch using the BrainLab positioning box. Treatment was executed after image verification with two-dimensional/two-dimensional matching of kilovoltage–kilovoltage planar images or 3D matching of cone-beam CT acquired with the Varian OBI system (version 1.4) installed at the linear accelerator.

RapidArc plans were optimized for multiple arcs of variable length for a Clinac 2100iX equipped with a Millennium-120 MLC (120 leaves with a resolution at isocenter of 5 mm for the inner 20 cm and 10 mm for the outer 2 × 10 cm) and a photon beam energy of 6 MV. Further details on the RapidArc technique can be