Radiotherapy and Oncology 123 (2017) 251–256

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Arteriovenous malformations

Dynamic conformal arc radiosurgery for arteriovenous malformations: Outcome and influence of clinical and dosimetrical data

Karen Clement-Colmou [a,*], Vincent Roualdes [b], Stéphane-André Martin [b], Stephanie Josset [c], Hubert Desal [d], Loïc Campion [e], François Thillays [a]

[a] Radiation Oncology, Integrated Center of Oncology, Saint-Herblain; [b] Neurosurgery, Centre Hospitalier Universitaire, Nantes; [c] Medical Physics, Integrated Center of Oncology, Saint-Herblain; [d] Neuroradiology, Centre Hospitalier Universitaire, Nantes; and [e] Statistics, Integrated Center of Oncology, Saint-Herblain, France

ARTICLE INFO

Article history:
Received 18 February 2016
Received in revised form 9 March 2017
Accepted 10 March 2017
Available online 25 March 2017

Keywords:
Radiosurgery
Arteriovenous malformation
Linac
Stereotactic radiotherapy
Novalis
Dynamic conformal arc radiotherapy

ABSTRACT

Purpose: To assess efficacy, toxicity, and their predictive factors for dynamic conformal arc arteriovenous malformations (AVM) stereotactic radiosurgery.
Method: Data concerning 90 consecutive patients were retrospectively studied. Clinical, radiological, dosimetrical data and quality indexes were computed.
Results: AVM median volume was 1.06 cc. Median prescribed dose was 22 Gy. Total occlusion was obtained for 69% of patients. Post-radiosurgery annual hemorrhage rate was 2.2%. Predictive factor for total occlusion was delivered dose. Undesirable events occurred for 28% of patients. Predictive factors for adverse events were AVM revealing mode with seizure or headache, age ≤ 28, AVM diameter ≥ 3 cm Spetzler–Martin score ≥ 4, V12 Gy ≥ 2 cc, large target volume and low homogeneity index ($p < 0.05$). Brain parenchymal radiological reactions concerned 23% of patients, and their predictive factors were AVM revelation by seizure, deep localization, AVM diameter ≥ 3 cm, Spetzler–Martin score ≥ 4, previous radiosurgery, numerous embolization, target volume, V12 Gy and low homogeneity index ($p < 0.05$).
Conclusion: Occlusion rate and toxicities are comparable to other series. Specific attention must be paid on pre-treatment clinical data, and target volume should be as small as possible, without reducing the delivered dose.
 Radiotherapy and Oncology 123 (2017) 251–256

Arteriovenous malformations (AVM) can cause brain hemorrhage in young patients [1–3]. When total obliteration is not possible with surgery or embolization, stereotactic radiosurgery (SRS) is the treatment of choice [4,5]. In this order, use of dedicated or adapted linear accelerators is increasing [6]. The Novalis system is one of them, using several non-coplanar dynamic conformal arcs to deliver the dose in the target while protecting healthy tissue. Considering that it is a recent technology, literature data are lacking. The aim of this study was to assess efficacy, toxicity, and predictive factors of the issue of Novalis AVM SRS in a large range of patients.

Methods

SRS and follow-up

All patients receiving SRS for an AVM from October 2005 to October 2012 were included. Brainlab stereotactic invasive frame was used. Planning-CT was systematically registrated with pretherapeutic arteriography (realized the same day, with the stereotactic frame) and MRI (realized the day before and rigid-registrated with Iplan® Automatic Image Fusion, Brainlab).

Target volume included emergence of drainage vein, efferent vessels, and excluded the afferent arteries. No margin was applied to define the PTV. Prescribed dose was usually 25 Gy at the 80%-isodose, but could be reduced if the healthy brain tissue receiving 12 Gy exceeded 15 cc. SRS was planned with 6 MV X-rays, spread in conformational non-coplanar arcs. Finer dose distribution adjustments were made by a medical physicist. The treatment Planning System was Brainscan 5.32 then IplanRTdose 3.0.2, 4.1.1 and 4.1.2. Calculation algorithm was Iplan Pencil Beam.

* Corresponding author.
E-mail addresses: kclementcolmou@gmail.com (K. Clement-Colmou), Vincent.roualdes@chu-nantes.fr (V. Roualdes), Stephaneandre.Martin@chu-nantes.fr (S.-A. Martin), Stephanie.Josset@ico.unicancer.fr (S. Josset), Hubert.Desal@chu-nantes.fr (H. Desal), Loic.Campion@ico.unicancer.fr (L. Campion), Francois.Thillays@ico.unicancer.fr (F. Thillays).

http://dx.doi.org/10.1016/j.radonc.2017.03.013
0167-8140/

Follow-up consisted of an MRI and medical appointment. First MRI was done 6 months after SRS, then annually until total AVM occlusion. AVM total occlusion was defined by lack of residual fistula. If achieved on MRI, total occlusion was confirmed by arteriography. Partial occlusion was considered as subtotal if there was only a punctual residual shunt on the MRI, or/and arteriography corresponding to a 90% or more reduction of the initial AVM volume. Brain parenchymal reaction on MRI imaging (PR) was graded according to Nataf's scale [7], (Supplementary Table 1A).

Dosimetrical data

AVM target volume (TV), prescription isodose, prescribed dose, number of isocenter, number of dynamic arcs, prescription isodose volume (IV), AVM volume covered by prescription isodose (TIV), average dose, median, minimal and maximal doses (Dmin and Dmax), maximal dose received by 2% of TV (D2%), minimal dose received by 98% of TV (D98%), volume of healthy brain tissue receiving 12 Gy (V12) and 20 Gy (V20) were retrospectively collected on the original approved treatment plan. Quality indexes were calculated [8–12], (Supplementary Table 1B).

Statistics

Quantitative variables were described by median [range] or mean ± standard deviation. Qualitative variables were described by respective distribution modalities. Follow-up was calculated as the duration between SRS and event or the last known date without event. Event-free survival curves were calculated with the Kaplan–Meier method. At the univariate step, EFS prognostic value was determined using Log rank test (qualitative parameters) or univariate Cox model (continuous parameters). Multivariate analyses were done with Cox semi-parametric model. All analyses were done in a two-sided way and $p < 5\%$ was considered significant. Statistical calculations were done using Stata 13.1 SE software (StataCorp, College Station, Texas).

Results

Patients and SRS

Ninety patients were included. Average follow-up duration was 54 months (16–94). Patient's characteristics are resumed in Table 1. Previous embolization concerned 53 patients (58.9%) (1–8 sequences, median 2).

Dosimetrical results are resumed in Table 2.

SRS efficacy and fails

Total AVM occlusion occurred in 58 patients (69%) in a median time of 30,4 months (5–73). Subtotal occlusion occurred for 12 patients. Occlusion rate was not different for previously embolized or non embolized patients (Fig. 1B). Nine patients underwent cerebral hemorrhage. Two of them bled within the month following SRS, before any SRS occlusive effect. For the other patients, median time between SRS and hemorrhage were 26 months (3–67). Annual hemorrhage rate after SRS was 2.2%.

Predictive factors for AVM occlusion were prescribed dose ($p = 0.014$), average, median, maximal and minimal doses. A 22 Gy cut-off could be highlighted (Fig. 1C). Clinical, radiological and other dosimetrical data were not predictive for efficacy.

Undesirable events

Twenty-five patients experienced 32 undesirable events. Seizure concerned 16 patients, in average 19.9 months after SRS (1–43 months). Eight patients showed headache, within 16.7 months (6–32). Six patients suffered from definitive handicap, occurring 13–28 months after SRS: 3 visual field defects, 1 hemiparesis, 1 sensitive defect and 1 cognitive deficit.

Table 1
Patient's and AVM's characteristics.

Characteristics	Number (%)
Women/Men	40 (44)/50 (66)
Age (average)	35 (9–72)
AVM	
Size > 3 cm	14 (16)
Superficial/deep localization	55 (61)/35 (39)
Frontal	25 (28)
Temporal	18 (20)
Occipital	17 (19)
Parietal	13 (14)
Periventricular	9 (10)
Infratentorial	8 (9)
Venous drainage	
Single/multiple	24 (27)/66 (73)
Superficial	37 (41)
Deep	18 (20)
mixt	35 (39)
Arterial aneurysm	13 (14)
Venous aneurysm	13 (14)
Hemorrhage	43 (48)
Hemorrhage stigmata (MRI)	45 (50)
Clinical symptoms:	
Seizure	23 (26)
Headache	22 (24)
Other	12 (13)
Fortuitous	2 (2)
Previous treatment	61 (67)
Average time before SRS	427 days (35–4011)
Embolization	46 (51)
Surgery	4 (4)
SRS	3 (3)
Embolization + surgery	3 (3)
Embolization + SRS	4 (4)
Surgery + SRS	1 (1)
Spetzler–Martin score	
1	17 (19)
2	37 (41)
3	30 (33)
4	6 (7)
≥5	0 (0)
RBAS sore (median)	1.02 ± 0.37

Table 2
Dosimetric data results.

Characteristics	Number
AVM volume (TV)	Median 1.06 cc (0.01–11.1)
Arc number	Median 5 (4–10)
Conformation	
Dose to 80% isodose (D80)	Median 22 Gy (14–25)
80% isodose Volume (IV)	Médiane 1.6 cc (0.1–14.7)
Target volume covered by 80% isodose (TIV)	95.4 ± 4.6%
C Brainlab index	1.6 ± 0.3
Conformation relative to target Index (IV/TV)	1.6 ± 1.1
Conformation and volume Index CV (TIV/TV)	1 ± 0.05
Conformation and tissue Index CT (TIV/IV)	0.7 ± 0.13
Paddick Index (CVxCT)	0.6 ± 0.1
Dose to Target	
Dmean	24.7 ± 2.4
Dmax	27.4 ± 2.6
D2%	27.4 ± 2.5
D98%	21.2 ± 2.4
Dmin	17.5 ± 3.3
Dose distribution	
V12	Median 3.6 cc (0.2–22.2)
V20	Median 0.9 cc (0–5.5)
Homogeneity Index (Dmax/D80)	1.3 ± 0.02
Covering Index (Dmin/D80)	0.8 ± 0.1
Gradient Index (V40%/IV)	3.8 ± 0.9