

1.

Year: 2006

Patient number: 38

Author: Cohen, Gadol Aaron A.; Pollock, Bruce E.

Reference: Journal of neurosurgery, 104, 6Suppl, 388-91, 2006

Title: Radiosurgery for arteriovenous malformations in children

Abstract:OBJECT: The authors present the results of stereotactic radiosurgery performed in a consecutive series of children with arteriovenous malformations (AVMs) and analyze factors associated with successful radiosurgery for this condition.

METHODS: Between 1990 and 2001, 38 patients 18 years of age or younger underwent radiosurgery for AVMs. The median patient age was 15 years; 20 patients (53%) had experienced a prior hemorrhage. Twenty-seven AVMs (71%) were Spetzler-Martin Grade III or higher; 16 patients (42%) had AVMs located in the basal ganglia, thalamus, or brainstem. The median AVM volume was 3.4 cm³. The median radiosurgery-based AVM score was 1.08 according to the following formula: AVM score = 0.1 volume (cm³) + 0.02 x age (years) + 0.3 x location (frontal/temporal = 0; parietal/occipital/corpus callosum/cerebellar = 1; basal ganglia/thalamus/brainstem = 2). The median follow-up period was 42 months. One patient (3%) had an intraventricular hemorrhage 26 months after radiosurgery but experienced no new deficit. No patient had a permanent radiation-related complication after radiosurgery. Twenty-six patients (68%) had excellent outcomes (as defined by complete obliteration of the AVM with no new deficit) after radiosurgical treatment (21 cases determined using angiography and five using magnetic resonance imaging). Twelve patients (32%) remained unchanged (incomplete obliteration but no new deficit). Univariate analysis found that patient age, AVM volume, location, or Spetzler-Martin grade did not correlate with excellent outcomes. Patients whose radiosurgery-based AVM scores were 1 or lower experienced an excellent outcome more frequently than patients with an AVM score higher than 1 (88% compared with 52%, p = 0.03). CONCLUSIONS: Radiosurgery was successful in the treatment of the majority of pediatric patients suffering from AVMs, and morbidity levels were minimal. The radiosurgery-based AVM grading scale accurately predicted these outcomes. Children whose AVMs are obliterated after radiosurgery should undergo repeated angiography after they reach adulthood to rule out the possibility of a recurrent nidus that would expose them to an ongoing risk of hemorrhage.

2.

Year: 2006

Patient number: 40

Author: Nagaraja, S.; Lee, K. J.; Coley, S. C.; Capener, D.; Walton, L.; Kemeny, A. A.; Wilkinson, I. D.; Griffiths, P. D.

Reference: Neuroradiology, 48, 11, 821-829, 2006

Title: Stereotactic radiosurgery for brain arteriovenous malformations: Quantitative MR assessment of nidus response at 1 year and angiographic factors predicting early obliteration

Abstract:Introduction: We investigated the role of magnetic resonance angiography (MRA) in the early follow-up of patients after stereotactic radiosurgery (STRS) for cerebral arteriovenous malformations (AVMs) and determined the influence of individual morphological factors of AVMs in early response to treatment. Methods: A group of 40 patients (41 AVMs) consented to a dedicated 1.5-T MR protocol 12 months after receiving STRS for a brain AVM. In addition to standard spin echo sequences, 3-D contrast-enhanced sliding interleaved Ky MRA (CE-SLINKY) and dynamic time-resolved subtraction angiography (MR-DSA) were performed. Nidal volumes were calculated using CE-SLINKY data in patients with a persisting arteriovenous shunt. Planning angiographic data was investigated in all 40 patients. The following AVM factors were used in the statistical analysis to determine their role in nidus obliteration: (1) maximum linear dimension, (2) nidal volume, (3) AVM location (4) nidal morphology, (5) venous drainage, (6) high-flow angiographic change, (7) prior embolization, and (8) dose reduction. Results: Complete nidal obliteration was found in 9 patients, 26 showed greater than 50% nidal reduction and 6 had less than 50%. Two AVM factors, venous drainage and AVM location, were found to significantly correlate with rate of obliteration. Conclusion: We successfully demonstrated the use of MRA to quantitatively assess the response of AVMs to STRS. Two AVM factors, venous drainage and AVM location were found to correlate with rate of obliteration prior to the application of the Bonferroni correction, but if this more rigorous statistical test was applied then none of the factors was found to be significant. © Springer- Verlag 2006.

3.

Year: 2006

Patient number: 372

Author: Nicolato, Antonio; Lupidi, Francesco; Sandri, Marco F.; Foroni, Roberto; Zampieri, Piergiuseppe; Mazza, Carlo; Maluta, Sergio; Beltramello, Alberto; Gerosa, Massimo

Reference: International journal of radiation oncology biology physics, 64, 3, 904-13, 2006

Title: Gamma knife radiosurgery for cerebral arteriovenous malformations in children/adolescents and adults Part I: Differences in epidemiologic, morphologic, and clinical characteristics, permanent complications, and bleeding in the latency period

Abstract:PURPOSE: To compare the epidemiologic, morphologic, and clinical characteristics of 92 children/adolescents (Group A) and 362 adults (Group B) with cerebral arteriovenous malformations (cAVMs) considered suitable for radiosurgery; to correlate radiosurgery-related permanent complication and post-radiosurgery bleeding rates in the 75 children /adolescents and 297 adults available for follow-up. METHODS AND MATERIALS: Radiosurgery was performed with a model C 201-source Co60 Leksell Gamma Unit (Elekta Instruments, Stockholm, Sweden). Fisher exact two-tailed, Wilcoxon rank-sum, and two-sample binomial exact tests were used for statistical analysis. RESULTS: There were significant differences between the two populations in sex ($p = 0.015$), clinical presentation ($p = 0.001$), and location ($p = 0.008$). The permanent complication rate was lower in younger (1.3%) than in older patients (5.4%), although the

difference was not significant ($p = 0.213$). The postradiosurgery bleeding rate was lower in Group A (1.3%) than in Group B (2.7%) ($p = 0.694$), with global actuarial bleeding rates of 0.56% per year and 1.15% per year, respectively. **CONCLUSIONS:** The different characteristics of child/adolescent and adult cAVMs suggest that they should be considered two distinct vascular disorders. The similar rates of radiosurgery-related complications and latency period bleeding in the two populations show that gamma knife radiosurgery does not expose young patients to a higher risk of sequelae than that for older patients.

4.

Year: 2006

Patient number: 255

Author: Nicolato, Antonio; Lupidi, Francesco; Sandri, Marco F.; Foroni, Roberto; Zampieri, Piergiuseppe; Mazza, Carlo; Pasqualin, Alberto; Beltramello, Alberto; Gerosa, Massimo

Reference: International journal of radiation oncology biology physics, 64, 3, 914-21, 2006

Title: Gamma Knife radiosurgery for cerebral arteriovenous malformations in children/adolescents and adults Part II: Differences in obliteration rates, treatment-obliteration intervals, and prognostic factors

Abstract: **PURPOSE:** To evaluate and compare obliteration rates (OBRs) and treatment-obliteration intervals (TOIs) for cerebral arteriovenous malformations (cAVMs) treated with Gamma Knife radiosurgery in children/adolescents and adults; and to determine factors predicting the OBR and TOI in these two populations. **METHODS AND MATERIALS:** This study concerned 62 children/adolescents and 193 adults observed for $> \text{ or } = 3$ years. Fisher exact two-tailed and Wilcoxon rank-sum tests, multiple logistics, and Cox proportional hazard models were used for statistical analysis. **RESULTS:** The overall OBR was 85.5% in children /adolescents and 87.6% in adults ($p = 0.671$), but children/adolescents showed higher 36-month actuarial OBRs (69.35%) and shorter median TOIs (25.7 months) than adults (66.84% and 28.2 months; $p = 0.006$ and $p = 0.017$, respectively). In children/adolescents, lower Spetzler-Martin grades ($p = 0.043$) and younger age ($p = 0.019$) correlated significantly with OBRs, and lower Spetzler-Martin grades ($p = 0.024$) and noneloquent cAVM locations ($p = 0.046$) with TOIs. In adults, low flow through the cAVM and $< 6.2\text{-cm}^3$ volume were associated with both OBR and TOI ($p = 0.012$ and $p = 0.002$, respectively). **CONCLUSIONS:** The differences in OBRs within 3 years and TOIs, although slight, seem to show that pediatric cAVMs behave differently from those in adults after Gamma Knife radiosurgery.

5.

Year: 2006

Patient number: 243

Author: Pollock, Bruce E.; Brown, Robert D., Jr.

Reference: Neurology, 67, 9, 1630-4, 2006

Title: Use of the Modified Rankin Scale to assess outcome after arteriovenous malformation radiosurgery

Abstract:OBJECTIVE: To present the results of arteriovenous malformation (AVM) radiosurgery using the Modified Rankin Scale (MRS) as the primary outcome measure and to analyze whether previous AVM rupture or other factors have an effect on outcomes after AVM radiosurgery. METHODS: We reviewed outcomes after AVM radiosurgery for 243 patients from 1990 and 2001. The mean follow-up after radiosurgery was 65 months. RESULTS: Forty-one patients (17%) sustained a decline in MRS (median -2) after AVM radiosurgery. We noted a decline in MRS in 4% of patients 1 year after radiosurgery, 8% of patients at 3 years after radiosurgery, and 15% of patients at 7 years after radiosurgery. The radiosurgery-based AVM score correlated with a decline in MRS after AVM radiosurgery in multivariate testing (odds ratio 2.1; 95% CI 1.2 to 3.6; $p < 0.01$). CONCLUSIONS: Previous AVM rupture did not influence neurologic deterioration after AVM radiosurgery. The radiosurgery-based AVM score predicted the chance of a worse MRS after radiosurgery.

6.

Year: 2006

Patient number: 288

Author: Sheehan, Jason; Yen, Chun Po; Steiner, Ladislau

Reference: Journal of Neurosurgery, 105, 2, 325-329, 2006

Title: Gamma knife surgery-induced meningioma - Report of two cases and review of the literature

Abstract:Gamma Knife surgery (GKS) is a minimally invasive neurosurgical technique. During the past 30 years, radiosurgery has been performed for a number of intracranial disorders with a generally low incidence of side effects. Although radiation-induced neoplasia following radiotherapy is well documented, there are few reports of this complication following radiosurgery. The authors are engaged in an ongoing project in which they are studying the delayed adverse effects of radiosurgical changes in 2500 patients with arteriovenous malformations (AVMs) treated within a 30-year period. The cases of 1333 patients treated by the senior author (L.S.) have been reviewed thus far. A subset of 288 patients in this group underwent neuroimaging and participated in clinical follow up for at least 10 years. The authors report two cases of radiosurgically induced neoplasia. In both cases the patient was treated with GKS for an AVM. Longer than 10 years after GKS, each of the patients was found to have an incidental, uniformly enhancing, dura-based mass lesion near the site of the AVM. These lesions displayed the imaging characteristics of a meningioma. Because in both cases the lesion has displayed no evidence of a mass effect, they continue to be followed using serial neuroimaging. These are the fifth and sixth cases meeting the criteria for radiation-induced neoplasms defined by Cahan, et al., in 1998. Although radiosurgery is generally considered quite safe, the incidence of radiation-induced neoplasms is not known. These cases and the few others detailed in the literature emphasize the need for long-term neurosurgical follow-up review in patients after radiosurgery.

7.

Year: 2006

Patient number: 28

Author: Sirin, Sait; Kondziolka, Douglas; Niranjan, Ajay; Flickinger, John C.; Maitz, Ann H.; Lunsford, L. Dade

Reference: Neurosurgery, 58, 1, 17-27, 2006

Title: Prospective staged volume radiosurgery for large arteriovenous malformations: indications and outcomes in otherwise untreatable patients

Abstract: **OBJECTIVE:** The obliteration response of an arteriovenous malformation (AVM) to radiosurgery is strongly dependent on dose and volume. For larger volumes, the dose must be reduced for safety, but this compromises obliteration. In 1992, we prospectively began to stage anatomic components in order to deliver higher single doses to symptomatic AVMs >15 ml in volume. **METHODS:** During a 17-year interval at the University of Pittsburgh, 1040 patients underwent radiosurgery for a brain AVM. Out of 135 patients who had multiple procedures, 37 patients underwent prospectively staged volume radiosurgery for symptomatic otherwise unmanageable larger malformations. Twenty-eight patients who were managed before 2002 were included in this study to achieve sufficient follow-up in assessing the outcomes. The median age was 37 years (range, 13-57 yr). Thirteen patients had previous hemorrhages and 13 patients had attempted embolization. Separate anatomic volumes were irradiated at 3 to 8 months (median, 5 mo) intervals. The median initial AVM volume was 24.9 ml (range, 10.2-57.7 ml). Twenty-six patients had two stages and two had three-stage radiosurgery. Seven patients had repeat radiosurgery after a median interval of 63 months. The median target volume was 12.3 ml. (range, 4.2-20.8 ml.) at Stage I and 11.5 ml. (range, 2.8-22 ml.) at Stage II. The median margin dose was 16 Gy at both stages. Median follow-up after the last stage of radiosurgery was 50 months (range, 3-159 mo). **RESULTS:** Four patients (14%) sustained a hemorrhage after radiosurgery; two died and two patients recovered with mild permanent neurological deficits. Worsened neurological deficits developed in one patient. Seizure control was improved in three patients, was stable in eight patients and worsened in two. Magnetic resonance imaging showed T2 prolongation in four patients (14%). Out of 28 patients, 21 had follow-up more than 36 months. Out of 21 patients, seven underwent repeat radiosurgery and none of them had enough follow-up. Of 14 patients followed for more than 36 months, seven (50%) had total, four (29%) near total, and three (21%) had moderate AVM obliteration. **CONCLUSIONS:** Prospective staged volume radiosurgery provided imaging defined volumetric reduction or closure in a series of large AVMs unsuitable for any other therapy. After 5 years, this early experience suggests that AVM related symptoms can be stabilized and anticipated bleed rates can be reduced.

8.

Year: 2005

Patient number: 28

Author: Aoyama, Hidefumi; Shirato, Hiroki; Katoh, Norio; Kudo, Kohsuke; Asano, Takeshi; Kuroda, Satoshi; Ishikawa, Tatsuya; Miyasaka, Kazuo

Reference: International journal of radiation oncology biology physics, 62, 4, 1232-8, 2005

Title: Comparison of imaging modalities for the accurate delineation of arteriovenous malformation, with reference to stereotactic radiosurgery

Abstract: Purpose: To investigate the discrepancy between the arteriovenous malformations seen on magnetic resonance angiography (MRA) and on stereotactic digital subtracted angiography (DSA). Methods and Materials: The target volume on stereotactic DSA (V(DSA)) and the target volume on MRA (V(MRA)) were separately delineated in 28 intracranial arteriovenous malformations. The coordinates of the center and the outer edges of V(DSA) and V(MRA) were calculated and used for the analyses. Results: The standard deviations (mean value) of the displacement of centers of V(MRA) from V(DSA) were 2.67 mm (-1.82 mm) in the left-right direction, 3.23 mm (-0.08 mm) in the anterior-posterior direction, and 2.16 mm (0.91 mm) in the craniocaudal direction. V(MRA) covered less than 80% of V(DSA) in any dimensions in 9 cases (32%), although no significant difference was seen in the target volume between each method, with a mean value of 11.9 cc for V(DSA) and 12.3 cc for V(MRA) ($p = 0.948$). Conclusion: The shift of centers between each modality is not negligible. Considering no significant difference between V(DSA) and V(MRA), but inadequate coverage of the V(DSA) by V(MRA), it is reasonable to consider that the target on MRA might include the feeding artery and draining vein and possibly miss a portion of the nidus.

9.

Year: 2005

Patient number: 41

Author: Ganz, J. C.; Reda, W. A.; Abdelkarim, K.; Hafez, A.

Reference: Journal of Neurosurgery, 102, SUPPL., 4-7, 2005

Title: A simple method for predicting imaging-based complications following gamma knife surgery for cerebral arteriovenous malformations

Abstract: Object. The authors studied the relationship between dose planning parameters and complications in the treatment of cerebral arteriovenous malformations (AVMs). Methods. There were 41 continuous unselected patients. The mean follow-up period was 19 months; the mean age was 28 years; the male/female ratio was 2.2:1.0; the median prescription dose was 25 Gy (range 14-25 Gy); the median prescription isodose was 50%. The median lesion volume was 4.4 cm³ (3). The median lesion coverage was 93%; and the mean conformity index was 1.22. The authors found no relationship between lesion volume or integral dose and the development of the clinical effects based on the adverse radiation effects (AREs); however, there was a significant relationship between both target volume and integral dose with the development of AREs as well as the severity of the AREs. Conclusions. The integral dose could be used as a guideline for the prescription dose. Arguments are made for maximizing the prescription dose for the long-term safety of the patient.

10.

Year: 2005

Patient number: 463

Author: Gerosa, M.; Nicolato, A.; Foroni, R.; Lupidi, F.; Visca, A.; Beltramello, A.; Bricolo, A.

Reference: Rivista Medica, 11, 1-2, 39-42, 2005

Title: Intracranial arterio-venous malformations Gamma Knife radiosurgery as a primary therapeutic option

Abstract: During the last decades, Gamma Knife radiosurgery has gained considerable momentum in the therapeutic armamentarium for intracranial arterio-venous malformations, basically because of the validating clinical results and the low incidence of side effects. The Authors present their experience (1993-2004) in 463 crucially located lesions. At a mean angiographical follow-up of 36 months the overall rate of complete obliteration was 84%, partial obliteration was observed in 13%, unchanged nidus size in 2% and volume progression in 1%. Clinical outcome was quite rewarding. Best clinical and radiological results were observed in the group of patients with smaller artero-venous malformations, treated directly by Gamma Knife radiosurgery, whereas the group of patients with larger nidus volumes - mostly treated with combined procedures - showed less gratifying results. Statistically, the most significant volume cut-off was estimated to be very close to 10 cc. Staged radiosurgery might provide new options to this regard. Copyright © 2005 by new Magazine edizioni s.r.l.

11.

Year: 2005

Patient number: 1203

Author: Hung, Chuan P. A. N.; Sheehan, J.; Stroila, M.; Steiner, M.; Steiner, L.

Reference: Journal of Neurosurgery, 102, SUPPL., 124-127, 2005

Title: Late cyst formation following gamma knife surgery of arteriovenous malformations

Abstract: Object. The authors present data concerning the development of cysts following gamma knife surgery (GKS) in 1203 consecutive patients with arteriovenous malformations (AVMs) treated by the senior author (L.S.). The cyst was defined as a fluid-filled cavity at the site of a treated AVM. Cases involving regions corresponding to previous hematoma cavities were excluded. The incidence of cyst formation was assessed using magnetic resonance imaging studies performed in 196 cases with more than 10 years of follow up, in 332 cases with 5 to 10 years of follow up, and in 675 cases with less than 5 years of follow up. One hundred five cases were lost to follow-up study. The Cox regression method was used to analyze the factors related to cyst formation. Methods. The incidence of cyst formation in the entire patient population was 1.6 and 3.6% in those undergoing follow-up examination for more than 5 years. Ten of 20 cysts developed between 10 to 23 years, nine between 5 to 10 years, and one in less than 5 years following the treatment. Cyst fluid aspiration, cystoperitoneal shunt placement, or

craniotomy were used in three symptomatic cases. Analysis of age, sex, and treatment parameters yielded no significant relationship with cyst formation; however, radiation-induced tissue change following GKS ($p = 0.027$) and prior embolization ($p = 0.011$) were related to cyst formation. Conclusions. Overall, the incidence of cyst formation in patients who underwent GKS for AVM was 1.6%. The development of the cyst was related to the duration of the follow-up period. When cysts are symptomatic, surgical intervention should be performed.

12.

Year: 2005

Patient number: 237

Author: Izawa, M.; Hayashi, M.; Chernov, M.; Nakaya, K.; Ochiai, T.; Murata, N.; Takasu, Y.; Kubo, O.; Hori, T.; Takakura, K.

Reference: Journal of Neurosurgery, 102, SUPPL., 34-37, 2005

Title: Long-term complications after gamma knife surgery for arteriovenous malformations

Abstract: Object. The authors analyzed of the long-term complications that occur 2 or more years after gamma knife surgery (GKS) for intracranial arteriovenous malformations (AVMs). Methods. Patients with previously untreated intracranial AVMs that were managed by GKS and followed for at least 2 years after treatment were selected for analysis (237 cases). Complete AVM obliteration was attained in 130 cases (54.9%), and incomplete obliteration in 107 cases (45.1%). Long-term complications were observed in 22 patients (9.3%). These complications included hemorrhage (eight cases), delayed cyst formation (eight cases), increase of seizure frequency (four cases), and middle cerebral artery stenosis and increased white matter signal intensity on T(2)-weighted magnetic resonance imaging (one case of each). The long-term complications were associated with larger nidus volume ($p < 0.001$) and a lobar location of the AVM ($p < 0.01$). Delayed hemorrhage was associated only with incomplete obliteration of the nidus ($p < 0.05$). Partial obliteration conveyed no benefit. Delayed cyst formation was associated with a higher maximal GKS dose ($p < 0.001$), larger nidus volume ($p < 0.001$), complete nidus obliteration ($p < 0.01$), and a lobar location of the AVM ($p < 0.05$). Conclusions. Incomplete obliteration of the nidus is the most important factor associated with delayed hemorrhagic complications. Partial obliteration does not seem to reduce the risk of hemorrhage. Complete obliteration can be complicated by delayed cyst formation, especially if high maximal treatment doses have been administered.

13.

Year: 2005

Patient number: 500

Author: Maruyama, Keisuke; Kawahara, Nobutaka; Shin, Masahiro; Tago, Masao; Kishimoto, Junji; Kurita, Hiroki; Kawamoto, Shunsuke; Morita, Akio; Kirino, Takaaki

Reference: The New England journal of medicine, 352, 2, 146-53, 2005

Title: The risk of hemorrhage after radiosurgery for cerebral arteriovenous malformations
Abstract:BACKGROUND: Angiography shows that stereotactic radiosurgery obliterates most cerebral arteriovenous malformations after a latency period of a few years. However, the effect of this procedure on the risk of hemorrhage is poorly understood. METHODS: We performed a retrospective observational study of 500 patients with malformations who were treated with radiosurgery with use of a gamma knife. The rates of hemorrhage were assessed during three periods: before radiosurgery, between radiosurgery and the angiographic documentation of obliteration of the malformation (latency period), and after angiographic obliteration. RESULTS: Forty-two hemorrhages were documented before radiosurgery (median follow-up, 0.4 year), 23 during the latency period (median follow-up, 2.0 years), and 6 after obliteration (median follow-up, 5.4 years). As compared with the period between diagnosis and radiosurgery, the risk of hemorrhage decreased by 54 percent during the latency period (hazard ratio, 0.46; 95 percent confidence interval, 0.26 to 0.80; P=0.006) and by 88 percent after obliteration (hazard ratio, 0.12; 95 percent confidence interval, 0.05 to 0.29; P<0.001). The risk was significantly reduced during the period after obliteration, as compared with the latency period (hazard ratio, 0.26; 95 percent confidence interval, 0.10 to 0.68; P=0.006). The reduction was greater among patients who presented with hemorrhage than among those without hemorrhage at presentation and similar in analyses that took into account the delay in confirming obliteration by means of angiography and analyses that excluded data obtained during the first year after diagnosis. CONCLUSIONS: Radiosurgery significantly decreases the risk of hemorrhage in patients with cerebral arteriovenous malformations, even before there is angiographic evidence of obliteration. The risk of hemorrhage is further reduced, although not eliminated, after obliteration. Copyright 2005 Massachusetts Medical Society.

14.

Year: 2005

Patient number: 32

Author: Maruyama, Keisuke; Shin, Masahiro; Tago, Masao; Kurita, Hiroki; Kawamoto, Shunsuke; Morita, Akio; Kirino, Takaaki

Reference: Journal of neurosurgery, 102, 49-52, 2005

Title: Gamma knife surgery for arteriovenous malformations involving the corpus callosum

Abstract:OBJECT: The purpose of this study was to evaluate the safety and efficacy of gamma knife surgery (GKS) for the treatment of arteriovenous malformations (AVMs) involving the corpus callosum. METHODS: Thirty-two patients aged from 7 to 65 years (median 25 years) with AVMs of the corpus callosum underwent GKS between 1990 and 2002. The maximum AVM diameter was more than 3 cm in 11 patients (34%). The AVM volume ranged from 0.1 to 19.1 cm³ (median 1.6 cm³). The median dose to the AVM margin was 20 Gy (range 17-28 Gy). Patients were followed for 1 to 12 years (median 9 years). The angiographically confirmed actuarial obliteration rate was 64% and 74% at 4 and 6 years, respectively. Younger patient age ($p < 0.05$) and lower radiosurgery-based grading score (calculated from the patient age and AVM volume; $p < 0.01$) were the

significant factors affecting successful AVM obliteration. No patient suffered a hemorrhage after GKS, although 28 patients (88%) had a history of hemorrhage from their AVMs. Radiation-induced neurological deficit was observed only in one patient (3%) who had undergone previous radiotherapy (50 Gy). No patient experienced complications of occlusion or stenosis of the normal vascular structures adjacent to the AVM.

CONCLUSIONS: Gamma knife surgery is a safe and effective treatment for selected patients with AVMs involving the corpus callosum, and it carries a low risk of damaging adjacent critical vascular structures. Even ruptured AVMs with relatively large diameter can be successfully treated, especially in younger patients, with minimal morbidity and a low risk of repeated hemorrhage.

15.

Year: 2005

Patient number: 63

Author: Nicolato, Antonio; Foroni, Roberto; Seghedoni, Andrea; Martines, Valentina; Lupidi, Francesco; Zampieri, Piergiuseppe; Sandri, Marco F.; Ricci, Umberto; Mazza, Carlo; Beltramello, Alberto; Gerosa, Massimo; Bricolo, Albino

Reference: Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery, {Childs-Nerv-Syst}, Apr 2005 (epub: 15 Jan 2005), vol. 21, no. 4, p. 301-7; discussion 308, ISSN: 0256-7040.

Title: Leksell gamma knife radiosurgery for cerebral arteriovenous malformations in pediatric patients

Abstract: **OBJECTS:** The authors report their experience of gamma knife radiosurgery (GKR) in a large series of pediatric cerebral arteriovenous malformations (cAVMs). The advantages, risks and failures of this approach are presented and discussed. **METHODS:** Gamma knife radiosurgery was performed on 63 children aged < or =16 years. Haemorrhage was the clinical onset in 50 out of 63 cases. The mean pre-GK cAVM volume was 3.8 cm(3). Fifty-eight out of 63 cAVMs were Spetzler-Martin grades I-III. Most lesions (47 out of 63) were in eloquent or deep-seated brain regions. **CONCLUSION:** Gamma knife radiosurgery-related complications occurred in 2 out of 47 cases with an available follow-up (1 had transient and 1 permanent morbidity). No bleeding occurred during the latency period. In 39 children with >36- month follow-up, complete cAVM occlusion was angiographically documented in 31, with a 3- and 4-year actuarial obliteration rate of 72 and 77% respectively. High rates of complete obliteration and very low frequency of permanent morbidity with no bleeding during the latency period encourage widespread application of GKR in the treatment of pediatric cAVMs.

16.

Year: 2005

Patient number: 1203

Author: Pan, Hung Chuan; Sheehan, Jason; Stroila, Matei; Steiner, Melita; Steiner, Ladislau

Reference: Journal of neurosurgery, 102, 124-7, 2005

Title: Late cyst formation following gamma knife surgery of arteriovenous malformations

Abstract:OBJECT: The authors present data concerning the development of cysts following gamma knife surgery (GKS) in 1203 consecutive patients with arteriovenous malformations (AVMs) treated by the senior author (L.S.) . The cyst was defined as a fluid-filled cavity at the site of a treated AVM. Cases involving regions corresponding to previous hematoma cavities were excluded. The incidence of cyst formation was assessed using magnetic resonance imaging studies performed in 196 cases with more than 10 years of follow up, in 332 cases with 5 to 10 years of follow up, and in 675 cases with less than 5 years of follow up. One hundred five cases were lost to follow-up study. The Cox regression method was used to analyze the factors related to cyst formation. METHODS: The incidence of cyst formation in the entire patient population was 1.6 and 3.6% in those undergoing follow-up examination for more than 5 years. Ten of 20 cysts developed between 10 to 23 years, nine between 5 to 10 years, and one in less than 5 years following the treatment. Cyst fluid aspiration, cystoperitoneal shunt placement, or craniotomy were used in three symptomatic cases. Analysis of age, sex, and treatment parameters yielded no significant relationship with cyst formation; however, radiation-induced tissue change following GKS ($p = 0.027$) and prior embolization ($p = 0.011$) were related to cyst formation. CONCLUSIONS: Overall, the incidence of cyst formation in patients who underwent GKS for AVM was 1.6%. The development of the cyst was related to the duration of the follow-up period. When cysts are symptomatic, surgical intervention should be performed.

17.

Year: 2005

Patient number: 236

Author: Shin, Masahiro; Kawahara, Nobutaka; Maruyama, Keisuke; Tago, Masao; Ueki, Keisuke; Kirino, Takaaki

Reference: Journal of neurosurgery, 102, 5, 842-6, 2005

Title: Risk of hemorrhage from an arteriovenous malformation confirmed to have been obliterated on angiography after stereotactic radiosurgery

Abstract:OBJECT: Radiosurgery has been widely adopted for the treatment of cerebral arteriovenous malformations (AVMs) in which the practical endpoint is angiographic evidence of obliteration, presumed to be consistent with elimination of the risk of hemorrhage. To test this unverified assumption, the authors followed 236 radiosurgery-treated AVMs between 1 and 133 months (median 77 months) after angiographic evidence of obliteration. METHODS: Four patients experienced hemorrhage between 16 and 51 months after angiographic confirmation of AVM obliteration, and two underwent resection. The histological findings in these patients showed occlusion of the AVM by thickening of the intimal layer with dense hyalinization as well as a small amount of residual AVM vessels and a tiny vasculature. The risks of hemorrhage from these presumably obliterated AVMs were 0.3% for the annual bleeding risk and 2.2% for the cumulative risk over 10 years. Continuous enhancement of the nidus on computerized tomography (CT) or magnetic resonance (MR) imaging was the only significant factor positively associated with hemorrhage in the statistical analysis ($p =$

0.0212). **CONCLUSIONS:** Because the study was based on limited follow-up data, its significance for defining predictive features of hemorrhage after angiographic evidence of obliteration is still indeterminable. Nevertheless, disappearance of the AVM on angiography after radiosurgery does not always indicate total elimination of the disease, especially when CT or MR imaging continues to demonstrate an enhancing lesion. The authors therefore recommend continual follow up even after evidence of AVM obliteration on angiography.

18.

Year: 2004

Patient number: 18

Author: Guo, Wan Yuo; Pan, Hung Chi; Wu, Hsiu Mei; Hsieh, Wanhwa A.; Tsai, Mong Hsun; Chow, Yau Mei; Chung, Wen Yu; Shiau, Cheng Ying; Chen, Shin Kuang; Chang, Wushou P.

Reference: Journal of radiation research, 45, 2, 269-74, 2004

Title: Individuals' leukocyte DNA double-strand break repair as an indicator of radiosurgery responses for cerebral arteriovenous malformations

Abstract: To evaluate the feasibility of using radiosensitivity of peripheral leukocytes as a predictor of clinical therapeutic responses to radiosurgery in individuals with cerebral arteriovenous malformation (AVM), we enrolled 18 patients years after they had received Gamma Knife radiosurgery for their cerebral AVM. The AVMs were shown with different degrees of regression in size in posttherapeutic periods. The peripheral leukocytes of these patients were collected at the last neuroimaging follow-ups. The leukocytes, before and 1 and 2 h after 8 Gy external gamma-irradiation, were evaluated for the amounts of DNA double-strand breaks (DSB) in 50 randomly selected individual nuclei by the neutral single cell gel electrophoresis, or so-called comet analysis. After being adjusted for gender and age at radiosurgery, the individuals with less posttherapeutic regression in AVM sizes or relatively poor or inadequate responses to radiosurgery were shown to have significantly higher DSB repair capacity on their leukocytes by comet analysis. These results suggested that in vitro radiosensitivity of peripheral leukocytes may provide valuable information for predicting therapeutic response or for adjusting irradiation doses in AVM radiosurgery.

19.

Year: 2004

Patient number: 19

Author: Guo, Wan Yuo; Wu, Yu Te; Wu, Hsiu Mei; Chung, Wen Yuh; Kao, Yi Hsuan; Yeh, Tzu Chen; Shiau, Cheng Ying; Pan, D. Hung Chi; Chang, Yue Cune; Hsieh, Jen Chuen

Reference: AJNR. American journal of neuroradiology, 25, 10, 1636-44, 2004

Title: Toward normal perfusion after radiosurgery: perfusion MR Imaging with independent component analysis of brain arteriovenous malformations

Abstract: BACKGROUND AND PURPOSE: Brain perfusion is disturbed by cerebral

arteriovenous malformations (AVMs). Our study was conducted to determine the radiosurgical effects on this disturbed perfusion. **METHODS:** MR perfusion imaging with independent component analysis was performed in five healthy subjects and 19 patients with AVM before and after radiosurgery (every 6 months up to 2 years). Perfusion map relative cerebral blood volume (rCBV), cerebral blood flow (rCBF), and mean transient time (rMTT) were assessed. Regions of interest (ROIs) on AVM target sections were defined as follows: N, AVM nidus; H, the rest of the ipsilateral hemisphere; P, immediately posterior to the nidus; A, immediately anterior to the nidus; Ar, anterior remote; Pr, posterior remote. Similar ROIs in the contralateral hemisphere (N1, H1, P1, A1, Pr1, and Ar1) served as internal references. Perfusion ratios of ROI-ROI1 were defined. Nonparametric Mann-Whitney U tests and generalized linear models were used for statistical analysis. **RESULTS:** Before radiosurgery, patients' H/H1 rCBV and rCBF ratios were significantly higher than those of healthy subjects ($P < .005$), indicating AVM steal. Three types of perilesional perfusion disturbance were observed. From the first postradiosurgical follow-up at 6 months, N/N1 rCBV and rCBF ratios gradually decreased to 1.0 (both $P < .001$), whereas rMTT ratios gradually increased to 1.0 ($P < .015$); H/H1, A/A1, and P/P1 rCBV and rCBF ratios decreased after radiosurgery ($P < .005$), indicating reversal of steal toward normal perfusion. **CONCLUSION:** Initial high transnidus flow and perinidal perfusion disturbances were demonstrated. They gradually changed toward normal perfusion after radiosurgery. This explains, in part, the pathophysiologic factors of AVM and therapeutic effects.

20.

Year: 2004

Patient number: 50

Author: Konya, D.; Kiliç, T.; Peker, S.; Cekirge, S.; Baltacıoğlu, F.; Pamir, M. N.

Reference: Turk Serebrovaskuler Hastalıklar Dergisi, 10, 1, 51-56, 2004

Title: Results of deeply situated intracranial AVM's treated with gamma knife

Abstract: Deeply situated intracranial arteriovenous malformations have more mortality and morbidity ratios, as they present anatomical difficulties in surgical approaches. On the other hand, technically, deep location is not a complication increasing factor in radiosurgery. In this prospective study, first 50 patients with deep AVM's who have at least 2 year follow-up after gamma-knife treatment are evaluated. All 50 deep situated AVM's revealed a decrease in their nidus volumes. In 44 (88%) cases AVM occlusion was complete, 4 AVM's (8%) showed 50-80% decrease in their nidus volumes, and 2 other (4%) displayed only venous drainage. Six (12%) AVM cases demonstrated radiological T2 image changes around the AVM nidus, in the normal brain tissue, in 3 (6%) cases these changes caused neurologically permanent deficits. No mortality was detected in the deeply located AVM's and only one intracranial hemorrhage was detected in the latent period.

21.

Year: 2004

Patient number: 50

Author: Maruyama, Keisuke; Kondziolka, Douglas; Niranjan, Ajay; Flickinger, John C.; Lunsford, L. Dade

Reference: Journal of neurosurgery, 100, 3, 407-13, 2004

Title: Stereotactic radiosurgery for brainstem arteriovenous malformations: factors affecting outcome

Abstract:OBJECT: Management options for arteriovenous malformations (AVMs) of the brainstem are limited. The long-term results of stereotactic radiosurgery for these disease entities are poorly understood. In this report the authors reviewed both neurological and radiological outcomes following stereotactic radiosurgery for brainstem AVMs over 15 years of experience. METHODS: Fifty patients with brainstem AVMs underwent gamma knife surgery between 1987 and 2002. There were 29 male and 21 female patients with an age range of 7 to 79 years (median 35 years). Anatomical locations of these AVMs included the midbrain (39 lesions), pons (20 lesions), and medulla oblongata (three lesions). The radiation dose applied to the margin of the AVM varied from 12 to 26 Gy (median 20 Gy). Forty-five patients were followed up from 5 to 176 months (mean 72 months). The angiographically confirmed actuarial obliteration rate was 66% at the final follow-up examination. Two patients experienced a hemorrhage before obliteration. The annual hemorrhage rate was 1.7% for the first 3 years after radiosurgery and 0% thereafter. Patients who had received irradiation at two or fewer isocenters had higher obliteration rates (80% compared with 44% for > two isocenters, $p = 0.006$), and this was related to a more spherical nidus shape. The rate of persistent neurological complications in patients treated using magnetic resonance imaging-based dose planning after 1993 was 7%, compared with 20% in patients treated before 1993. An older patient age, a lesion located in the tectum, and a higher radiosurgery-based score were significantly associated with greater neurological complications. CONCLUSIONS: Stereotactic radiosurgery provided complete obliteration of AVMs in two thirds of the patients with a low risk of latency- interval hemorrhage. Better three-dimensional imaging studies and conformal dose planning reduced the risk of adverse radiation effects. Younger patients harboring more spherical AVMs that did not involve the tectal plate had the best outcomes.

22.

Year: 2004

Patient number: 56

Author: Pollock, Bruce E.; Gorman, Deborah A.; Brown, Paul D.

Reference: Journal of neurosurgery, 100, 2, 210-4, 2004

Title: Radiosurgery for arteriovenous malformations of the basal ganglia, thalamus, and brainstem

Abstract:OBJECT: Although stereotactic radiosurgery is frequently performed for arteriovenous malformations (AVMs) in deep locations, outcomes after radiosurgery for these patients have not been well studied. The goal of this paper was to study these outcomes. METHODS: Between 1990 and 2000, 56 patients underwent radiosurgery for

AVMs located in the basal ganglia (10 patients), thalamus (30 patients), or brainstem (16 patients). The median age of these patients was 34.2 years. Thirty-five patients (62%) had experienced previous bleeding. The AVMs were classified Grade IIIB in 62% of patients and Grade IV in 38% according to the modified Spetzler-Martin Scale; the median radiosurgery-based AVM score was 1.83. The median volume of the lesion was 3.8 cm³ and the median radiation dose delivered to its margin was 18 Gy. The median duration of follow-up review after radiosurgery was 45 months (range 3-121 months). In seven patients (12%) hemorrhage occurred at a median of 12 months after radiosurgery; five patients (9%) died and two recovered without any deficit. Permanent radiation-related complications occurred in six (12%) of 51 patients (excluding the five patients who died of hemorrhage) after one procedure and in three (18%) of 17 patients after repeated radiosurgery. Obliteration of the AVM was noted in 24 patients (43%; obliteration was confirmed by angiography in 18 patients and by magnetic resonance (MR) imaging in six patients) after a single procedure and in 32 patients (57%; confirmed by angiography in 25 patients and by MR imaging in seven patients) after one or more procedures. Excellent outcomes (obliteration of the lesion without any new deficit) were obtained in 39% of patients after one radiosurgical procedure and in 48% after one or more procedures. Twelve (67%) of 18 patients with AVM scores lower than 1.5 had excellent outcomes compared with 15 (39%) of 38 patients with AVM scores greater than 1.5 ($p = 0.053$). **CONCLUSIONS:** Less than half of the patients with deeply located AVMs were cured of the future risk of hemorrhage without new neurological deficits. This experience emphasizes the difficulty in treating patients with deeply located AVMs; the majority of whom are also poor candidates for resection or embolization.

23.

Year: 2004

Patient number: 65

Author: Schäuble, B.; Cascino, G. D.; Pollock, B. E.; Gorman, D. A.; Weigand, S.; Cohen, Gadol A. A.; McClelland, R. L.

Reference: Neurology, 63, 4, 683-7, 2004

Title: Seizure outcomes after stereotactic radiosurgery for cerebral arteriovenous malformations

Abstract: **OBJECTIVES:** To determine the effect of stereotactic radiosurgery on seizure outcomes for patients with intracerebral arteriovenous malformations (AVM). **METHODS:** Between May 1990 and December 1998, 65 patients with a history of single or recurrent seizures underwent AVM radiosurgery, had more than 1 year of follow-up, and sufficient data to record an Engel seizure frequency score. The authors reviewed their records and updated clinical information when necessary with direct patient contact. Follow-up ranged from 12 to 144 months (median, 48 months). Seizure frequency was compared before and after radiosurgery with the Engel Seizure Frequency Scoring System. **RESULTS:** Overall, 26 patients (51%) were seizure-free (aura-free) after radiosurgery at 3-year follow-up; 40 patients (78%) had an excellent outcome (non-disabling simple partial seizures only) at 3-year follow-up. Factors associated with seizure-free or excellent outcomes include a low seizure frequency score (<4) before radiosurgery and smaller

size and diameter AVM. Twenty-three patients had intractable partial epilepsy prior to treatment. Twelve (52%) of 23 and 11 of 18 (61%) patients with medically intractable partial epilepsy had excellent outcomes at years 1 and 3. **CONCLUSION:** Overall, stereotactic radiosurgery improves seizure outcomes in the majority of patients and more than half of the patients with medically intractable partial epilepsy had an excellent seizure outcome after radiosurgery.

24.

Year: 2004

Patient number: 400

Author: Shin, Masahiro; Maruyama, Keisuke; Kurita, Hiroki; Kawamoto, Shunsuke; Tago, Masao; Terahara, Atsuro; Morita, Akio; Ueki, Keisuke; Takakura, Kintomo; Kirino, Takaaki

Reference: Journal of neurosurgery, 101, 1, 18-24, 2004

Title: Analysis of nidus obliteration rates after gamma knife surgery for arteriovenous malformations based on long-term follow-up data: the University of Tokyo experience

Abstract:**OBJECT:** A large number of clinical studies have been made on treatment outcomes of radiosurgery for arteriovenous malformations (AVMs), but the reported obliteration rates following this treatment vary significantly, perhaps reflecting the different methods and timings of the imaging studies used. **METHODS:** The authors retrospectively analyzed their experience with gamma knife surgery in 400 patients with AVMs (follow-up period 1-135 months, median 65 months), with special reference to the imaging modality used in each case. The calculated obliteration rates varied from 68.2 to 92%, depending on imaging modality and timing of evaluation. When only unquestionable imaging data such as demonstrations of a residual nidus on computerized tomography (CT) or magnetic resonance (MR) images or findings on angiograms were used in the calculation, the obliteration rates were 72% at 3 years and 87.3% at 5 years. Factors leading to a better obliteration rate were previous hemorrhage ($p = 0.0084$), smaller nidus ($p = 0.0023$), and higher radiation dose to the lesion's margin ($p = 0.0495$), as determined in a multivariate analysis. Factors leading to an earlier obliteration of the nidus were male sex ($p = 0.0001$), previous hemorrhage ($p = 0.0039$), smaller nidus diameter ($p = 0.0006$), and dose planning using angiography alone ($p = 0.0201$). **CONCLUSIONS:** After the introduction of CT and MR images into dose planning, the conformity and selectivity of dosimetry improved remarkably, although the latency intervals until obliteration were prolonged. Imaging outcomes for AVMs should be evaluated using data provided by longer follow-up periods. The timing of additional treatments for residual AVMs should be decided cautiously, considering the size of the AVM, the patient age and sex, and the history of hemorrhage before radiosurgery.

25.

Year: 2004

Patient number: 57

Author: Yu, Cheng; Petrovich, Zbigniew; Apuzzo, Michael L. J.; Zelman, Vladimir;

Giannotta, Steven L.

Reference: Neurosurgery, 54, 5, 1104, 2004

Title: Study of magnetic resonance imaging-based arteriovenous malformation delineation without conventional angiography

Abstract:OBJECTIVE: In this study, we aimed to assess the feasibility of arteriovenous malformation (AVM) delineation for gamma knife radiosurgery without conventional angiography and to correlate factors that may affect AVM delineation. METHODS: A series of 57 consecutive patients with AVMs treated with gamma knife radiosurgery from August 1994 to December 2000 were reviewed. All patients in the study had undergone pretreatment angiography. The mean AVM volume was 2.8 cm³, with a median of 2.0 cm³ (range, 0.04-22 cm³). All AVMs were delineated on the original frame-based magnetic resonance imaging (MRI) scans by a vascular neurosurgeon without the assistance of angiography and then compared with the actual AVM delineation on the basis of previously performed angiography and MRI. Univariate correlation analysis was used to determine the relationship of AVM coverage, size, diffuseness, previous embolization, and hemorrhage parameters. RESULTS: The study volume or MRI-based volume alone coincided with the actual treatment volume by a mean of 58% for diffuse and 87% for nondiffuse AVMs (P = 0.0005). At AVM volume greater than 2 cm³, the median percentage of coinciding volume was 63% for embolized AVMs and 82% for nonembolized AVMs (P = 0.0315). Conversely, the study volume overestimated the actual treatment volume by a mean of 57% for AVMs larger than 2 cm³ versus 25% for AVMs smaller than 2 cm³ (P = 0.0012). In general, the percentage of the coinciding volume was inversely related to that of the excess volume, whereas both the study volume and the coinciding volume were proportionate to AVM volume at treatment. CONCLUSION: MRI-based AVM delineation without conventional angiography may be feasible only for selected patients, such as those with nondiffuse and large nonembolized AVMs.

26.

Year: 2003

Patient number: 144

Author: Pollock, Bruce E.; Gorman, Deborah A.; Coffey, Robert J.

Reference: Neurosurgery, 52, 6, 1291-6, 2003

Title: Patient outcomes after arteriovenous malformation radiosurgical management: results based on a 5- to 14-year follow-up study

Abstract:OBJECTIVE: Radiosurgery is commonly performed for patients with small to medium-sized arteriovenous malformations (AVMs). However, few articles present overall outcomes after one or more radiosurgical procedures, and few data are available for periods longer than 5 years after AVM radiosurgery. METHODS: Between 1990 and 1997, 144 patients underwent AVM radiosurgery and had angiographic follow-up. Of these patients, 112 (78%) had Spetzler-Martin Grade III or greater AVMs; 37 (26%) were located in the basal ganglia, thalamus, or brainstem. Twenty-six patients (18%) underwent repeat radiosurgery. The mean follow-up of 15 patients who died as a result of

AVM bleeding or underwent AVM resection after the initial radiosurgery was 22 months (range, 3-47 mo); the mean follow-up of the remaining 129 patients was 86 months (range, 23-169 mo). RESULTS: Excellent (obliteration without deficit, n = 96) or good (obliteration with minor deficit, n = 9) outcomes were achieved in 73% of patients after one or more radiosurgical procedures. Twenty patients (14%) sustained major deficits (n = 15; five had obliteration) or died (n = 5) after radiosurgery. Sixteen patients (11%) had unchanged neurological examinations but persistent arteriovenous shunting. Five patients (4%) required surgery (cystoperitoneal shunting, n = 1; AVM resection, n = 4) at a median of 65 months after radiosurgery because of symptomatic cyst formation or persistent edema. The radiosurgery AVM score correlated with both excellent ($R(2) = -0.93$, $P = 0.003$) and excellent or good ($R(2) = -0.92$, $P = 0.004$) outcomes. CONCLUSION: The majority of AVM patients are protected from the risk of future hemorrhage and continue their normal daily activities after radiosurgery. Late complications requiring treatment are rare but can occur many years after patients are considered cured of their AVMs. Overall outcomes after AVM radiosurgery seem to be predicted accurately by the described method.

27.

Year: 2003

Patient number: 18

Author: Zhang, Xiao Qing; Shirato, Hiroki; Aoyama, Hidefumi; Ushikoshi, Satoshi; Nishioka, Takeshi; Zhang, Da Zhen; Miyasaka, Kazuo

Reference: International journal of radiation oncology biology physics, 57, 5, 1392-9, 2003

Title: Clinical significance of 3D reconstruction of arteriovenous malformation using digital subtraction angiography and its modification with CT information in stereotactic radiosurgery

Abstract: PURPOSE: A three-dimensional (3D) reconstruction method of arteriovenous malformation (AVM) nidus from digital subtraction angiography (DSA) in combination with CT and/or MRI was developed, and its usefulness was evaluated in this study.

MATERIALS AND METHODS: The contour of the AVM nidus was delineated on two orthogonal projected DSA images. First, the volume and center of the AVM nidus were calculated in a classic DSA plan using three maximal lengths of the nidus in three perpendicular directions, assuming that the nidus had a prolate ellipsoid shape. Second, in the 3D-DSA plan, the contours of the AVM nidus on the two orthogonal projected DSA images were segmented to be compatible with the slice thickness of the CT image. Assuming that each segment of the nidus has an ellipsoid pillar shape, the volume and center of each segment were calculated. The volume and 3D shape of the nidus were calculated by 3D reconstruction in the 3D- DSA plan. Third, in the CT-DSA plan, the contour based on the segmented DSA was superimposed on the corresponding transaxial CT image slice by slice. The cylindrical shape of the nidus in the transaxial image was modified using the enhanced CT images in the CT- DSA plan. These three planning methods were compared using dose-volume statistics from real patients' data. Eighteen patients with intracranial AVMs in different brain locations who had been treated by radiosurgery were the subjects of this study. To examine the visibility (validity) of the

nidus on the CT image, the nidus was delineated on an enhanced CT image without DSA superposition in the CT plan and compared with the CT-DSA plan. RESULTS: The variance in the distance between coordinates determined by the CT plan and those determined by the classic DSA plan was significantly larger than the variance in the CT-DSA plan ($p < 0.0001$ for lateral, AP, and craniocaudal directions). The difference in the variance was not reduced by the addition of MRI ($p < 0.0001$ for each direction). The mean volume \pm SD of the nidus calculated was 5.9 ± 8.0 cm³ in the classic DSA plan, 4.0 ± 5.6 cm³ in the 3D-DSA plan, and 3.6 ± 5.2 cm³ in the CT-DSA plan. The 3D-DSA plan significantly reduced the mean nidus volume 31.8% \pm 12.7% from the classic DSA plan ($p = 0.0054$). The CT-DSA plan further significantly reduced the volume 9.8% \pm 8.8% from the 3D-DSA plan ($p = 0.0021$). The mean overlapping volume of the nidus between the CT plan and CT-DSA plan was 2.6 ± 4.3 cm³ (range 0.17-18.9), corresponding to 63.7% \pm 19.2% (range 11.4-85.3%) of the volume in the CT-DSA plan. CONCLUSIONS: The superposition of the segmented DSA information on CT was shown to be an important tool to determine the precise shape of the nidus and is suggested to be useful to reduce partial occlusion of the AVM or radiation complications in radiosurgery.

28.

Year: 2002

Patient number: 242

Author: Crocco, A.

Reference: Journal of neurosurgical sciences, 46, 2, 43-54, 2002

Title: Arteriovenous malformations in the basal ganglia region: Gamma Knife radiosurgery as first choice treatment in selected cases

Abstract:BACKGROUND: The authors report the results of Gamma Knife (GK) radiosurgery on a clinical series of selected patients with brain basal ganglia arteriovenous malformations (BG AVMs). Furthermore, clinico-epidemiological and anatomo-functional pictures of BG AVMs and supratentorial cortical AVMs are comparatively analyzed, and their influence on the radiosurgical outcome is discussed. METHODS: At our Department, 33 BG AVMs (21 with FU >2 years) and 209 cortical AVMs (110 with FU >2 years) with a radiosurgical volume 10 cc underwent GK from February 1993 to July 2001. Mean age, male/female ratio (M/F), and bleeding rate at clinical onset in the 2 subgroups of patients were as follows: 25.5 years (5-62 years), 16 M/17 F, and 30/33 (91%) in BG AVMs, respectively; 34.4 years (8-74 years), 124 M/85 F, and 107 /209 (51%) in cortical AVMs, respectively. Statistical analysis performed with contingency table method and deviance analysis according to generalized linear models showed that the differences concerning age at onset and bleeding rate were highly significant. RESULTS: The rates of complete obliteration, permanent morbidity, bleeding/rebleeding during latency period, and unsuccessful embolization attempt in the 2 subgroups of patients were as follows: 81%, 4%, 8%, and 41.7% in BG AVMs, respectively; 85.5%, 2%, 2%, and 2% in cortical AVMs, respectively. CONCLUSIONS: In our experience, the different clinico-epidemiological and anatomo-functional characteristics between BG AVMs and cortical AVMs do not seem to influence the radiosurgical outcome as complete obliteration and permanent neurological sequelae

rates are very similar in these 2 subgroups of patients. GK radiosurgery may be considered the first choice treatment modality in BG AVMs with <10 cc volume (very high cure rate, very low permanent morbidity, and zero mortality). Although the haemorrhagic onset in BG AVMs is much more frequent than in cortical AVMs, the difference in the bleeding/rebleeding rate between the 2 subgroups of patients during the latency period is not statistically significant and this occurrence seems to be limited within the first year after GK.

29.

Year: 2002

Patient number: 351

Author: Flickinger, John C.; Kondziolka, Douglas; Maitz, Ann H.; Lunsford, L. Dade

Reference: Radiotherapy and oncology, 63, 3, 347-54, 2002

Title: An analysis of the dose-response for arteriovenous malformation radiosurgery and other factors affecting obliteration

Abstract: PURPOSE: The aim of this study was to better understand arteriovenous malformation (AVM) obliteration rates after radiosurgery. METHODS AND MATERIALS: We studied obliteration after Gamma knife radiosurgery in 351 AVM patients with 3-11 years of follow-up imaging. The median marginal dose was 20 Gy (range: 12-30) and median treatment volume was 5.7 cm³ (range: 0.26-24). Stereotactic targeting was with angiography alone in 250 AVMs, and additional magnetic resonance (MR) imaging in 101 AVMs. RESULTS: We documented obliteration by angiography in 193/264 (73%) AVM, and by MR alone in 75/87 (86%) AVM for a 75% corrected obliteration rate. We identified persistent out- of-field nidus in 18% of embolized vs. 5% of non-embolized patients, (P = 0.006). Multivariate analysis correlated in-field obliteration with marginal dose (P < 0.0001) and sex (P < or = 0.026, but not for overall obliteration P = 0.19). A mathematical dose-response model for overall obliteration was constructed to generate a dose-response curve for AVM obliteration with a maximum overall obliteration rate of 88% and minimal improvement above 25 Gy. We could not define the value of alpha/beta for AVM obliteration to a level of statistical significance. CONCLUSION: The rate of AVM obliteration from radiosurgery depends on the marginal dose administered with a dose-response curve that reaches a maximum of approximately 88%. The dose- response plateau reflects problems with target definition which is made more difficult by prior embolization. Copyright 2002 Elsevier Science Ireland Ltd.

30.

Year: 2002

Patient number: 115

Author: Inoue, Hiroshi K.; Ohye, Chihiro

Reference: Journal of neurosurgery, 97, 5Suppl, 474-6, 2002

Title: Hemorrhage risks and obliteration rates of arteriovenous malformations after gamma knife radiosurgery

Abstract:OBJECT: The purpose of this study was to analyze the risk of hemorrhage and the obliteration rate after treatment of patients with arteriovenous malformations (AVMs). METHODS: Between 1991 and 1995, 115 patients were treated using gamma knife radiosurgery (GKS). Surgical planning was based on angiograms and three-dimensional images. The angiographic features of the AVMs and the risk factors for hemorrhage were then evaluated. Hemorrhages occurred in eight patients (7%) 7 to 42 months after GKS. Based on AVM morphology, the rates of hemorrhage were five (7.6%) of 66 for AVMs with a single draining vein, seven (14%) of 66 for AVMs with deep drainage, four (26.7%) of 15 for AVMs with a varix, four (28.6%) of 14 for AVMs with venous obstruction, eight (17.0%) of 47 for high-flow (shunt- and mixed-type) AVMs, and five (35.7%) of 14 for large AVMs with a volume of more than 10 cm³. No hemorrhages were observed in association with low-flow (moyamoya-type) AVMs in this series. Total AVM obliteration was achieved in 81.3% of 80 patients who underwent angiography. The obliteration rate was 91.3% for moyamoyatype AVMs and 67.6% for shunt- and mixed-type AVMs. Early obliteration within 12 months was achieved in 63% of the moyamoya-type AVMs. CONCLUSIONS: Moyamoya-type AVMs seem to be at risk for post-GKS hemorrhage. Intravascular embolization should be considered prior to GKS for mixed- and shunt-type AVMs in an attempt to reduce the hemodynamic stress and thereby decrease the risk of hemorrhage.

31.

Year: 2002

Patient number: 39

Author: Lai, Erica Ho Pik; Lun, Samuel Leung Cheong

Reference: Journal of neurosurgery, 97, 5Suppl, 471-3, 2002

Title: Impact on the quality of life of patients with arteriovenous malformations during the latent interval between gamma knife radiosurgery and lesion obliteration

Abstract:OBJECT: The aim of this study was to measure the quality of life (QOL) in patients with cerebral arteriovenous malformations (AVMs) receiving gamma knife treatment before total AVM obliteration. Quality of life was assessed as it related to the knowledge of rebleeding risk during the waiting period, AVM symptoms, and previous bleeding. METHODS: Thirty-nine patients age 18 years or older without other medical problems were asked to complete a questionnaire that included demographic variables, immediate effect of gamma knife radiosurgery, symptoms of AVM, previous hemorrhage, and the Duke-University of North Carolina Health Profile (63 items). CONCLUSIONS: The QOL of patients with cerebral AVM during the waiting period after undergoing gamma knife treatment was affected by irreversible physical disabilities rather than the knowledge of hemorrhage risk and bleeding experience.

32.

Year: 2002

Patient number: 47

Author: Miyachi, S.; Negoro, M.; Suzuki, O.; Hattori, K.; Kobayashi, N.; Kojima, T.; Yoshida, J.

Reference: Japanese Journal of Neurosurgery, 11, 10, 660-667, 2002

Title: Endovascular treatment of AVMs: Indication, strategy and clinical results

Abstract: We reviewed 70 arteriovenous malformations (AVMs) treated with embolization over 5 years and investigated the treatment strategies for virtual AVMs simulating various types and situations with a questionnaire sent to 17 affiliated hospitals. Of 70 patients with AVMs, 14 underwent postembolization surgical removal, and 47 underwent radiosurgery. Four patients were cured with total occlusion of their AVM by embolization alone. 61 patients achieved a more than 70% occlusion of the nidus. We observed 12 complications including 3 permanent and 9 temporary. Based on these data, we created the chart of treatment strategy for AVMs. There is an absolute indication of embolization for large, high flow AVMs as well as possible bleeding sources such as intranidal or feeder aneurysms. Deep-seated feeders must be embolized presurgically along with fistulous or high-flow feeders, and fistulous and meningeal feeders should be treated before radiosurgery. The nidus must be packed with embolic materials with no risk of recanalization. The responses to a questionnaire revealed the tendency of less aggressive surgical extirpation for difficult AVMs, and more dependence on radiosurgery with or without embolization. The general strategy with more than 70% of consensus was following three: 1) radiosurgery for small AVM without bleeding, 2) embolization plus radio-surgery for large AVM with ischemic events, and for large, eloquent one and deep-seated one with minor hemorrhage, 3) surgical removal for small, middle-sized AVM with large hematoma except for middle-sized eloquent and deep-seated ones. Although the improvements in radiosurgery may narrow the indication of embolization, it still plays an important role for high grade AVMs by enhancing the effectiveness of the secondary treatment. The indication of embolization should be decided taking various factors about the angioarchitecture of AVMs as well as the patients' situations into considerations. The safest multi-axial method should be used for the benefit of patients with AVMs.

33.

Year: 2002

Patient number: 242

Author: Nicolato, A.; Foroni, R.; Crocco, A.; Zampieri, P. G.; Alessandrini, F.; Bricolo, A.; Gerosa, M. A.

Reference: Minimally invasive neurosurgery, 45, 4, 211-23, 2002

Title: Gamma knife radiosurgery in the management of arteriovenous malformations of the Basal Ganglia region of the brain

Abstract: OBJECTIVES: The authors report the results of gamma knife (GK) radiosurgery on a clinical series of selected patients with basal ganglia arteriovenous malformations (BGAVMs) in the brain. Clinical, epidemiological, anatomical and functional characteristics of BGAVMs and of supratentorial cortical AVMs are comparatively analyzed, and their influence on radiosurgical outcome is discussed. METHODS: At our Department, 33 BGAVMs (21 with FU > 2 years) and 209 cortical AVMs (110 with FU > 2 years) with a radiosurgical volume \leq 10 cc were treated with GK between February

1993 and July 2001. Mean age, male /female ratio (M/F), and incidence of haemorrhagic onset in the two subgroups of patients were as follows: 25.5 years (5 - 62 years), 16 M /17 F, and 30/33 (91%) in BGAVMs; 34.4 years (8 - 74 years), 124 M/85 F, and 107/209 (51%) in cortical AVMs. Statistical analysis performed using the contingency table method and deviance analysis according to generalized linear models showed that the differences in age and incidence of haemorrhagic onset were highly significant. RESULTS: The rates of complete obliteration, permanent morbidity, bleeding /rebleeding during the latency period, and unsuccessful embolisation attempts in the two subgroups of patients were as follows: 81%, 4%, 8%, and 41.7%, respectively, in BGAVMs; 85.5%, 2%, 2%, and 2% in cortical AVMs. Statistical analysis did not show any significant difference between the two subgroups of patients in the rates of complete obliteration, permanent morbidity, or latency period bleeding /rebleeding, while difference in failed embolization rates resulted to be highly significant (P = 0.00003). CONCLUSIONS: In our experience, the different clinical, epidemiological and anatomico-functional characteristics of BGAVMs and cortical AVMs do not seem to influence the radiosurgical outcome, since complete obliteration and permanent neurological sequelae rates were very similar in these two subgroups of patients. GK may be considered the first choice treatment modality for BGAVMs with < 10 cc volume, since it offers a very high cure rate, very low permanent morbidity, and zero mortality. Although haemorrhagic onset is much more frequent in BGAVMs than in cortical AVMs, the difference between the bleeding/rebleeding rates in the two subgroups of patients during the latency period is not statistically significant, and seems to be limited to the first year after GK.

34.

Year: 2002

Patient number: 85

Author: Pedersen, P. H.; Baardsen, R.; Larsen, J. L.; Thorsen, F.; Wester, K.

Reference: Tidsskrift for den Norske Laegeforening, 122, 13, 1277-1280, 2002

Title: Stereotactic radiosurgery for cerebral arteriovenous malformations

Abstract:Background. Different treatment modalities are being used for cerebral arteriovenous malformations. Material and methods. We have evaluated the results of stereotactic radiosurgery on 85 patients (48 females) with median age 34.5 years (range 4-70 years) treated at Haukeland University Hospital in Norway in 1989-96. Median follow-up time was 7 years 3 months (range 51-144 months). Data were obtained retrospectively from patient files. Results. Haemorrhage was the initial symptom in 72 patients. The majority of lesions were located deep within the brain parenchyma or near critical structures. The minimum dose to the periphery of the malformation was 15 to 33.3 Gy in 30-70% isodose line according to the volume and location of the malformation. Complete obliteration was obtained in 65 of 85 malformations (77%) and in two of five patients who were retreated. 85% of the malformations smaller than 4 cm(3); 50% of those larger than 4 cm(3) were obliterated after the treatment. The majority of the malformations were obliterated between two and three years after radiation. Radiation-related side effects were observed in six patients. Five patients experienced new bleeding during follow-up. Interpretation. Small and medium-sized arteriovenous

malformations are successfully treated with stereotactic radiosurgery with an acceptable rate of radiation-related side effects and latency bleeding.

35.

Year: 2002

Patient number: 356

Author: Pollock, B. E.; Flickinger, J. C.

Reference: Journal of Neurosurgery, 96, 1, 79-85, 2002

Title: A proposed radiosurgery-based grading system for arteriovenous malformations

Abstract: Object. Radiosurgery is an effective treatment strategy for properly selected patients harboring arteriovenous malformations (AVMs). Grading scales that are currently used to predict patient outcomes after AVM resection are unreliable tools for the prediction of the results of AVM radiosurgery. Methods. A grading system was developed to predict outcomes following AVM radiosurgery, based on the multivariate analysis of data obtained in 220 patients treated between 1987 and 1991 (Group 1). The dependent variable in all analyses was excellent patient outcome (complete AVM obliteration without any new neurological deficit). The grading scale was tested on a separate set of 136 patients with AVMs treated between 1990 and 1996 at a different center (Group 2). One hundred twenty-one (55%) of 220 Group 1 patients had excellent outcomes. Multivariate analysis identified five variables related to excellent patient outcomes: AVM volume ($p = 0.001$), patient age ($p < 0.001$), AVM location ($p < 0.001$), previous embolization ($p = 0.02$), and number of draining veins ($p < 0.001$). Regression analysis modeling permitted removal of two significant variables (previous embolization and number of draining veins) and resulted in the following equation to predict patient outcomes after AVM radiosurgery: $\text{AVM score} = (0.1)(\text{AVM volume in cm}^3) + (0.02)(\text{patient age in years}) + (0.3)(\text{location of lesion: Frontal or temporal} = 0; \text{parietal, occipital, intraventricular, corpus callosum, cerebellar} = 1; \text{or basal ganglia, thalamic, or brainstem} = 2)$. Seventy-nine (58%) of 136 Group 2 patients had excellent outcomes. All variables in the model remained significant for the Group 2 patients: AVM volume ($p = 0.01$), patient age ($p = 0.01$), and AVM location ($p < 0.001$). Testing of the entire model on the Group 2 patients demonstrated that the AVM score could be used to predict patient outcomes after radiosurgery ($p < 0.0001$). All patients with an AVM score of 1 or lower had an excellent outcome compared with only 39% of patients with an AVM score higher than 2. The Spetzler-Martin grade ($p = 0.13$), the K index ($p = 0.26$), and the obliteration prediction index ($p = 0.21$) did not correlate with excellent patient outcomes. Conclusions. Despite significant differences in preoperative patient characteristics and dose prescription guidelines at the two centers, the proposed AVM grading system strongly correlated with patient outcomes after single-session radiosurgery for both patient groups. Although further testing of this model by independent centers using prospective methodology is still required, this system allows a more accurate prediction of outcomes from radiosurgery to guide choices between surgical and radiosurgical management for individual patients with AVMs.

36.

Year: 2002

Patient number: 100

Author: Shin, Masahiro; Kawamoto, Shunsuke; Kurita, Hiroki; Tago, Masao; Sasaki, Tomio; Morita, Akio; Ueki, Keisuke; Kirino, Takaaki

Reference: Journal of Neurosurgery, 97, 4, 779-784, 2002

Title: Retrospective analysis of a 10-year experience of stereotactic radiosurgery for arteriovenous malformations in children and adolescents

Abstract: Object: To obtain information essential to the decision to perform radiosurgery for arteriovenous malformations (AVMs) in children and adolescents, the authors retrospectively analyzed their experience with gamma knife surgery for AVMs in 100 patients ranging in age from 4 to 19 years. Methods: Follow-up periods ranged from 6 to 124 months (median 71 months), and the actuarial obliteration rates demonstrated by angiography were 84.1, 89.4, and 94.7% at 3, 4, and 5 years, respectively. Factors associated with better obliteration rates in univariate analysis included the following: a patient age of 12 years or younger; a mean nidus diameter of 2 cm or less; a nidus volume of 3.8 cm³ or less; a maximum diameter of the nidus less than 3 cm; and a Spetzler-Martin grade of III or less. Radiation-induced neuropathy was seen in four patients, and the risk factors were considered to be a nidus in the brainstem and a maximum radiation dose greater than 40 Gy. Hemorrhage developed during the latency interval in four patients, and one patient with a cerebellar AVM died of the hemorrhage. The annual bleeding rate was 1.5%. Feeding arteries located in the posterior cranial fossa and an AVM nidus located in the cerebellum were significantly associated with the risk of hemorrhage. After angiographically verified obliteration of the nidus, 51 patients continued to be observed from 1 to 110 months (median 67 months); hemorrhage developed in one patient 38 months after nidus obliteration. Conclusions: Radiosurgery is an acceptable treatment for small AVMs in children and adolescents in whom a higher obliteration rate can be achieved with lower risks of interval hemorrhage compared with the reported results in the general population. Careful follow-up observation seems to be required, however, even after angiographically verified obliteration.

37.

Year: 2002

Patient number: 40

Author: Smyth, Matthew D.; Sneed, Penny K.; Ciricillo, Samuel F.; Edwards, Michael S.; Wara, William M.; Larson, David A.; Lawton, Michael T.; Gutin, Philip H.; Mc Dermott, Michael W.

Reference: Journal of neurosurgery, 97, 1, 48-55, 2002

Title: Stereotactic radiosurgery for pediatric intracranial arteriovenous malformations: the University of California at San Francisco experience

Abstract: OBJECT: Stereotactic radiosurgery for arteriovenous malformations (AVMs) is an accepted treatment option, but few reports have been published on the results of this treatment in children. In this study the authors describe a series of pediatric patients with a minimum follow-up duration of 36 months. METHODS: From 1991 to 1997, 40 children

(26 boys and 14 girls) with AVMs were treated with radiosurgery at the University of California at San Francisco (UCSF). Follow-up information was available for 31 children (20 boys and 11 girls) in whom the median age at initial treatment was 11.2 years (range 3.4-17.5 years). The median follow-up duration was 60 months (range 6-99 months). Sixteen percent of the AVMs were Spetzler-Martin Grade II; 68%, Grade III; 10%, Grade IV; and 6%, Grade V. The mean volume of the AVMs was 5.37 cm³ and the median volume was 1.6 cm³. The mean marginal dose of radiation was 16.7 Gy and the median dose was 18 Gy (range 12-19 Gy). Angiography performed in 26 children confirmed obliteration of the AVM nidus in nine patients (35%), partial response in 16 patients (62%), and no response in one patient (4%). In five patients who refused angiography, magnetic resonance (MR) imaging revealed obliteration in two patients and partial response in three patients, bringing the overall obliteration rate associated with initial radiosurgery to 35%. Logistic regression analysis confirmed a significant correlation between marginal dose prescription and response ($p = 0.025$); in AVMs that received at least 18 Gy there was a 10-fold increase in the obliteration rate (63%) over AVMs that received a lower dose. Lesions smaller than 3 cm³ were associated with a six-fold increased obliteration rate (53%) over lesions larger than 3 cm³ (8%), but AVM volume was not a statistically significant predictor of response ($p = 0.09$). Twelve patients have since undergone repeated radiosurgery and are currently being followed up with serial

38.

Year: 2001

Patient number: 329

Author: Bhatnagar, A.; Flickinger, J. C.; Kondziolka, D.; Niranjan, A.; Lunsford, L. D.

Reference: International journal of radiation oncology biology physics, 51, 4, 969-73, 2001

Title: An analysis of the effects of smoking and other cardiovascular risk factors on obliteration rates after arteriovenous malformation radiosurgery

Abstract: **PURPOSE:** To assess the relationships of smoking and other cardiovascular disease risk factors (hypertension, diabetes, hypercholesterolemia, and gender) to rates of radiosurgery-induced obliteration of arteriovenous malformations (AVM). **METHODS AND MATERIALS:** We evaluated follow-up imaging and clinical data in 329 AVM patients who received gamma knife radiosurgery at the University of Pittsburgh between 1987 and 1994. There were 113 smokers, 29 hypertensives, 5 diabetics, 4 hypercholesterolemic, 159 male patients, and 170 female patients. All patients had regular clinical or imaging follow-up for a minimum of 3 years after radiosurgery. **RESULTS:** Multivariate analysis showed that smoking had no effect on AVM obliteration ($p > 0.43$). Hypertension, diabetes, and hypercholesterolemia had no discernible effect on AVM obliteration in this study ($p > 0.78$). However, females aged 12-49 had a statistically significant lower in-field obliteration rate than males (78% vs. 89%, $p = 0.0102$). **CONCLUSION:** Smoking has no effect on AVM obliteration. Hypertension, diabetes, and hypercholesterolemia had no discernible effect in this study. Further study is needed to establish whether estrogen has a vascular protective effect that could partially limit radiosurgical AVM obliteration, as suggested by this study.

39.

Year: 2001

Patient number: 242

Author: Crocco, A.; Nicolato, A.; Foroni, R.; Zampieri, P. G.; Bricolo, A.; Gerosa, M. A.

Reference: Rivista Medica, 7, 3-4, 89-110, 2001

Title: Gamma Knife radiosurgery in the management of arteriovenous malformations of brain basal ganglia region

Abstract:The authors report the results of Gamma Knife (GK) radiosurgery on a clinical series of selected patients with brain basal ganglia arteriovenous malformations (BGAVMs). Furthermore, clinico- epidemiological and anatomo-functional pictures of BGAVMs and supratentorial cortical AVMs are comparatively analyzed, and their influence on the radiosurgical outcome is discussed. At our Department, 33 BGAVMs (21 with FU > 2 years) and 209 cortical AVMs (110 with FU > 2 years) with a radiosurgical volume (less-than or equal to) 10 cc underwent GK from February 1993 to July 2001. Mean age, male/female ratio (M/F), and bleeding rate at clinical onset in the two subgroups of patients were as follows: 25.5 years (5-62 years) , 16 M/17 F, and 30/33 (91%) in BGAVMs, respectively; 34.4 years (8-74 years), 124 M/85 F, and 107/209 (51%) in cortical AVMs, respectively. Statistical analysis performed with contingency table method and deviance analysis according to generalized linear models showed that the differences concerning age at onset and bleeding rate were highly significant. The rates of complete obliteration, permanent morbidity, bleeding/rebleeding during latency period, and unsuccessful embolization attempt in the two sub groups of patients were as follows: 81%, 4%, 8%, and 41.7% in BGAVMs, respectively; 85.5%, 2%, 2% and 2% in cortical AVMs, respectively. In our experience, the different clinico-epidemiological and anatomo-functional characteristics between BGAVMs and cortical AVMs do not seem to influence the radiosurgical outcome as complete obliteration and permanent neurological sequelae rates are very similar in these two subgroups of patients. GK radiosurgery may be considered the first choice treatment modality, in BGAVMs with < 10 cc volume (very high cure rate, very low permanent morbidity, and zero mortality). Although the haemorrhagic onset in BGAVMs is much more frequent than in cortical AVMs, the difference in the bleeding/rebleeding rate between the two subgroups of patients during the latency period is not statistically significant and this occurrence seem to be limited within the first year after GK.

40.

Year: 2001

Patient number: 10

Author: Eder, H. G.; Leber, K. A.; Eustacchio, S.; Pendl, G.

Reference: Child's nervous system, 17, 6, 341-6, 2001

Title: The role of gamma knife radiosurgery in children

Abstract:OBJECTS: Despite advances in microneurosurgery, the surgical management

of deep-seated lesions is still associated with a high risk. Gamma knife radiosurgery (GKRS), however, has improved the outcome of cerebral tumors and arteriovenous malformations (AVMs) in delicate areas. **METHODS:** Between March 1992 and June 1998, 50 children (age 1-16 years) with intracranial lesions were treated with GKRS. There were 12 low-grade gliomas, 12 high-grade gliomas, 7 craniopharyngiomas, 3 hamartomas, 2 meningiomas of the skull base, 2 vestibular schwannomas, 1 pituitary adenoma, 1 choroid plexus papilloma, and 10 AVMs. The mean size of the pathologies was 4.6 cm³ (range: 0.21-25.5 cm³). A mean marginal dose of 16 Gy (8-25 Gy) was applied to a mean isodose surface of 50% (35-90%). Clinical and neuroradiological follow-up were analyzed for outcome. Follow-up periods of 45 of these patients ranged from 8 to 79 months (mean 36 months); 5 patients were lost to follow-up. Neoplasms decreased in size in 15 cases (41%), remained unchanged in 13 patients (35%), and increased in 9 cases (24%). AVMs obliterated in 3 children (38%) within 24 months. Neurological follow-up demonstrated improved clinical status in 7 patients (15.5%), stable neurological status in 31 cases (69%) and clinical deterioration in 7 patients (15.5%). The treatment was well tolerated and no complications occurred. **CONCLUSIONS:** GKRS represents a safe and effective treatment option for benign neoplasms or AVMs in pediatric patients and may extend survival times of children with malignant lesions.

41.

Year: 2001

Patient number: 33

Author: Hadjipanayis, C. G.; Levy, E. I.; Niranjan, A.; Firlik, A. D.; Kondziolka, D.; Flickinger, J. C.; Lunsford, L. D.; Friedman, W. A.; Connolly, E. S., Jr.; Gutin, P. H.; McDermott, M. W.

Reference: Neurosurgery, 48, 1, 70-77, 2001

Title: Stereotactic radiosurgery for motor cortex region arteriovenous malformations

Abstract: **OBJECTIVE:** The optimal management of arteriovenous malformations (AVMs) in critical brain locations remains controversial. To reduce the risk of an AVM hemorrhage and to enhance the possibility of preserving neurological function, stereotactic radiosurgery was performed in 33 patients with newly diagnosed or residual AVMs located within the motor cortex. The role of embolization also was examined. **METHODS:** During a 9-year study period, 33 patients with AVMs located primarily in the motor cortex region were treated with stereotactic radiosurgery. These patients were followed up radiographically for a minimum of 36 months, or less if obliteration was documented before 36 months had elapsed. Of the 33 patients, 9 underwent embolization and 1 underwent microsurgery before radiosurgery. Nine patients required a second radiosurgery. The mean AVM target volume was 4.35 cc, and the average radiation dose to the AVM margin was 20 Gy. The median follow-up was 36 months (range, 10-91 mo), and angiographic follow-up of eligible patients was performed 24 or 36 months after radiosurgery. **RESULTS:** Results were stratified by radiosurgical target volumes: less than 3 cc (Group 1), 3 to 10 cc (Group 2), and greater than 10 cc (Group 3). Overall (including second radiosurgery), 13 (87%) of 15 patients in Group 1 had complete obliteration confirmed by angiography. Nine (64%) of 14 patients in Group 2 exhibited

nidus obliteration, and one (25%) of four patients in Group 3 demonstrated obliteration on a magnetic resonance imaging scan. Eight patients (24%) underwent second-stage radiosurgery after angiography revealed a persistent AVM nidus; three patients demonstrated complete obliteration on follow-up angiography. The obliteration rate was higher (87%) for AVMs with less than 3 cc target volume and lower (56%) for those with target volumes larger than 3 cc. One patient experienced worsening neurological function after radiosurgery, and one died from delayed AVM hemorrhage during the latency period. No patient bled after angiographically confirmed AVM obliteration. **CONCLUSION:** Stereotactic radiosurgery is a successful and safe management option for patients with motor cortex AVMs. The obliteration of AVMs and the attendant low morbidity rates indicate a primary role for radiosurgery in these patients. Staged radiosurgery may be necessary to increase obliteration rates for larger AVMs or for those that are not obliterated after the first procedure.

42.

Year: 2001

Patient number: 1593

Author: Karlsson, B.; Lax, I.; Söderman, M.

Reference: International journal of radiation oncology biology physics, 49, 4, 1045-51, 2001

Title: Risk for hemorrhage during the 2-year latency period following gamma knife radiosurgery for arteriovenous malformations

Abstract: **PURPOSE:** Radiosurgery does not immediately obliterate an arteriovenous malformation (AVM), and the risk for hemorrhage still persists until the AVM is occluded. There is controversy about whether this risk is altered after as compared to before radiosurgery. The aim of this paper is to study this topic further and to suggest a model to predict the risk for posttreatment hemorrhage. **METHODS AND MATERIALS:** The incidence of hemorrhages within the first 24 months following Gamma Knife radiosurgery was studied retrospectively among 1593 AVM patients, and was related to patient, AVM, and treatment parameters. **RESULTS:** Fifty-six patients experienced a hemorrhage in the latency period, representing an average annual incidence of 1.8%. The incidence of posttreatment hemorrhage was related to the patient's age, AVM volume, minimum dose, and average dose delivered to the AVM nidus. Based on these observations, an equation was defined that could quantify the probability for a posttreatment hemorrhage to occur. **CONCLUSION:** A model that can predict the probability for a hemorrhage within the first 24 months after radiosurgery is presented. The risk is higher for larger AVMs and for older patients, and it is lower when higher doses of radiation are used.

43.

Year: 2001

Patient number: 35

Author: Majhail, N. S.; Chander, S.; Mehta, V. S.; Julka, P. K.; Ganesh, T.; Rath, G. K.

Reference: Stereotactic and functional neurosurgery, 76, 1, 36-46, 2001

Title: Factors influencing early complications following Gamma Knife radiosurgery A prospective study

Abstract: **PURPOSE:** The factors influencing early complications following Gamma Knife radiosurgery have not been definitely established. We report a prospective study evaluating the incidence of early complications (occurring within 3 months of radiosurgery) and various factors associated with early complications following stereotactic Gamma Knife radiosurgery for intracranial lesions. **PATIENTS AND METHODS:** Seventy- nine previously unirradiated consecutive adult patients (82 lesions: arteriovenous malformations 35, benign tumors 43, metastases 4) treated by Gamma Knife radiosurgery were studied between May 1997 and August 1998. The median target volume was 4.8 cm³. The median dose of 15 Gy was prescribed to the 50% isodose. Patients were evaluated clinically and radiologically (with CT/MRI/SPECT) at 3-month intervals for the 1st year and 6 monthly thereafter. Complications were further divided as immediate (occurring within 24 h) or acute (occurring from 1 day to 3 months). **RESULTS:** Early complications were observed in 19 /79 (24.0%) patients. These included immediate in 10 (12.7%) and acute complications in 9 (11.3%) patients and were characterized by headache, nausea/vomiting, vertigo and seizures. No severe early complications were observed. Radiological changes in the form of perilesional edema were seen in 8/82 (9.8%) lesions. Maximum target diameter >25 mm was the only factor significantly associated with early complications by univariate analysis ($p = 0.0335$). Multivariate analysis revealed maximum target diameter >25 mm and prescribed dose >20 Gy to be significantly associated with early complications ($p = 0.0442$ and $p = 0.0083$, respectively). **CONCLUSION:** Up to one fourth of the patients undergoing Gamma Knife radiosurgery for intracranial lesions can experience self-limiting early toxicity. The selection of targets with small diameter and volume may reduce the risk of early complications following Gamma Knife radiosurgery. Copyright 2002 S. Karger AG, Basel.

44.

Year: 2001

Patient number: 25

Author: Régis, J.; Massager, N.; Lévrier, O.; Dufour, H.; Porcheron, D.; Reyns, N.; Peragut, J. C.; Farnarier, P.

Reference: Neuro-Chirurgie, 47, 2-3 Pt 2, 291-7, 2001

Title: Gamma-knife radiosurgery for brainstem arteriovenous malformations Preliminary results

Abstract: **BACKGROUND AND PURPOSE:** Microsurgical resection have the advantage to be immediately effective according to bleeding risk and is the reference treatment for cerebral arteriovenous malformations. For cerebral arteriovenous malformations located in the brainstem gamma- knife radiosurgery due to its low invasivity is classically a first line treatment. We reviewed the Marseilles experience to assess the efficacy and safety of gamma-knife radiosurgery for brain stem arteriovenous malformations. **METHODS:** We analyzed retrospectively data of 45 patients with an arteriovenous malformation located in the brain stem treated in Marseilles by gamma-knife radiosurgery by between

07 /92 and 12/99. Mean age was 42 years, there were 5 children. Arteriovenous malformations were located in the pons or midbrain for the majority of the patients. Intraaxial lesion was found in 82% of patients. Hemorrhage prior to radiosurgery occurred in 75% of the patients. Gamma-knife procedure was the first treatment of the arteriovenous malformations for 29 patients (65%); previous surgery was performed in 34 patients (15%). Mean nidus volume was 550 mm³ (32-14 196 mm³). Mean margin dose was of 23 Gy (range 15-30 Gy). Follow up was available for 25 patients (mean 18 months). RESULTS: One patient presented a transient worsening of his neurological status, and 2 patients developed a fixed deficit. Two patients underwent rebleeding at an interval of 12 to 36 months after the gamma-knife procedure. At last angiographic follow-up (13 patients), the obliteration rate was 82% of the arteriovenous malformations. A second procedure was proposed to a patient with only partial occlusion at 3 years. CONCLUSIONS: Gamma-knife radiosurgery can achieve good obliteration rate of brain stem arteriovenous malformations with low morbidity and may be a valuable first-choice therapy for such arteriovenous malformations. A larger population and longer follow up are mandatory in order to confirm these preliminary results.

45.

Year: 2001

Patient number: NA abstract

Author: Söderman, M.; Rodesch, G.; Karlsson, B.; Lax, I.; Lasjaunias, P.

Reference: Acta neurochirurgica, 143, 8, 801-10, 2001

Title: Gamma knife outcome models as a reference standard in the embolisation of cerebral arteriovenous malformations

Abstract:BACKGROUND: We sought to utilise outcome models from Gamma Knife radiosurgery (GKRS) to cerebral arteriovenous malformations (AVM) as a reference standard in assessing the clinical outcome of embolisation, thus comparing the outcomes of two different management alternatives, in the same patients. METHODS: 87 consecutive patients with 88 AVM were admitted during 1997-1999 for initial embolisation of an AVM. The clinical outcomes were recorded prospectively. Angiography under stereotactic conditions with measurement of AVM volume was performed before and after embolisation. GKRS outcome models were used to predict obliteration rate, complication rate and risk of haemorrhage before and after embolisation. The clinical outcome of embolisation followed by predicted outcome of adjunct GKRS was then compared with the predicted outcome of GKRS as the only treatment. FINDINGS: Eight patients were subjected to microcatheterisation but not to embolisation. By the end of the study period, embolisation had been terminated in 55 patients out of 80 (69%). The predicted outcome of GKRS alone was 58 obliterations and 12 complications while that of the combined management was 58 obliterations and 15 complications. The difference was not significant on the $p < 0.1$ level. INTERPRETATION: Volume measurement from angiography and outcome models from Gamma Knife radiosurgery are useful as a reference standard in the management of AVM. Absolute volume reduction from embolisation is most prominent for AVM > 10 ml and thus facilitates subsequent radiosurgery. For AVM ≤ 10 ml, GKRS as the only treatment can be an alternative to

primary embolisation, particularly if no significant volume reduction or obviously beneficial effect of targeted embolisation is expected. Further prospective studies are needed to identify subgroups in which one treatment has advantages over the other.

46.

Year: 2000

Patient number: 22

Author: Bednarz, G.; Downes, B.; Werner, Wasik M.; Rosenwasser, R. H.

Reference: International journal of radiation oncology biology physics, 46, 5, 1149-54, 2000

Title: Combining stereotactic angiography and 3D time-of-flight magnetic resonance angiography in treatment planning for arteriovenous malformation radiosurgery

Abstract:**PURPOSE:** This study was initiated to evaluate the advantages of using three-dimensional time-of-flight magnetic resonance angiography (3D TOF MRA), as an adjuvant to conventional stereotactic angiography, in obtaining three-dimensional information about an arteriovenous malformation (AVM) nidus and in optimizing radiosurgical treatment plans. **METHODS AND MATERIALS:** Following angiography, contrast-enhanced MRI and MRA studies were obtained in 22 consecutive patients undergoing Gamma Knife radiosurgery for AVM. A treatment plan was designed, based on the angiograms and modified as necessary, using the information provided by MRA. The quantitative analysis involved calculation of the ratio of the treated volume to the MRA nidus volume (the tissue volume ratio (TVR)) for the initial and final treatment plans. **RESULTS:** In 12 cases (55%), the initial treatment plans were modified after including the MRA information in the treatment planning process. The mean TVR for the angiogram-based plans was 1.63 (range 1.17-2.17). The mean coverage of the MRA nidus by the angiogram-based plans was 93% (range 73-99%). The mean MRA nidus volume was 2.4 cc (range 0.6-5.3 cc). The MRA-based modifications resulted in increased conformity with the mean TVR of 1.46 (range 1.20-1.74). These modifications were caused by MRA revealing irregular nidi and/or vascular components superimposed on the angiographic projections of the nidi. In a number of cases, the information from MRA was essential in defining the nidus when the projections of the angiographic outlines showed different superior and/or inferior extent of the nidus. In two cases, MRA revealed irregular nidi, correlating well with the angiograms and showed that the angiographically acceptable plans undertreated 27% of the MRA nidus in one case and 18% of the nidus in the other case. In the remaining 10 cases (45%), both MRI and MRA failed to detect the nidus due to surgical clip artifacts and the presence of embolizing glue. **CONCLUSIONS:** The 3D TOF MRA provided information on irregular AVM shape, which was not visualized by angiography alone, and it was superior to MRI for defining the AVM nidus. However, when imaging artifacts obscured the AVM nidus on MRI and MRA, angiography permitted detection of AVM. Utilizing MRA as a complementary imaging modality to angiography increased accuracy of the AVM radiosurgery and allowed for optimal dose planning.

47.

Year: 2000

Patient number: 254

Author: Chang, J. H.; Chang, J. W.; Park, Y. G.; Chung, S. S.

Reference: Journal of neurosurgery, 93, Suppl 3, 96-101, 2000

Title: Factors related to complete occlusion of arteriovenous malformations after gamma knife radiosurgery

Abstract:OBJECT: The authors sought to evaluate the effects of gamma knife radiosurgery (GKS) on cerebral arteriovenous malformations (AVMs) and the factors associated with complete occlusion. METHODS: A total of 301 radiosurgical procedures for 277 cerebral AVMs were performed between December 1988 and December 1999. Two hundred seventy-eight lesions in 254 patients who were treated with GKS from May 1992 to December 1999 were analyzed. Several clinical and radiological parameters were evaluated. CONCLUSIONS: The total obliteration rate for the cases with an adequate radiological follow up of more than 2 years was 78.9%. In multivariate analysis, maximum diameter, angiographically delineated shape of the AVM nidus, and the number of draining veins significantly influenced the result of radiosurgery. In addition, margin radiation dose, Spetzler-Martin grade, and the flow pattern of the AVM nidus also had some influence on the outcome. In addition to the size, topography, and radiosurgical parameters of AVMs, it would seem to be necessary to consider the angioarchitectural and hemodynamic aspects to select proper candidates for radiosurgery.

48.

Year: 2000

Patient number: 10

Author: Ezura, M.; Takahashi, A.; Jokura, H.; Shirane, R.; Yoshimoto, T.

Reference: Journal of clinical neuroscience, 7, Suppl 1, 14-8, 2000

Title: Endovascular treatment of aneurysms associated with cerebral arteriovenous malformations: experiences after the introduction of Guglielmi detachable coils

Abstract:The authors have treated 172 patients with arteriovenous malformation (AVM) since 1993. Among them, 25 patients had aneurysms with a total number of 43. The aneurysms were divided into four groups; proper feeder aneurysm (4), flow-related distal aneurysm (beyond the circle of Willis or M1, 7), flow-related proximal aneurysm (26) and remote aneurysm (6). Guglielmi detachable coil (GDC) embolisation was performed in 12 patients with 15 aneurysms. Gamma knife radiosurgery for AVM was performed in 10 of those 12 patients. Two of the proper feeder aneurysms were embolised with liquid material, together with the corresponding part of the AVM. The other aneurysms were treated surgically (14) or observed (12). There was no bleeding from aneurysms after treatment. In conclusion, GDC embolisation is a useful treatment for aneurysms associated with AVM, especially if the AVM is treated by radiosurgery. Liquid embolisation of a proper feeder aneurysm is one of the treatment options. Ltd.

49.

Year: 2000

Patient number: 85

Author: Flickinger, J. C.; Kondziolka, D.; Lunsford, L. D.; Kassam, A.; Phuong, L. K.; Liscak, R.; Pollock, B.

Reference: International journal of radiation oncology biology physics, 46, 5, 1143-8, 2000

Title: Development of a model to predict permanent symptomatic postradiosurgery injury for arteriovenous malformation patients Arteriovenous Malformation Radiosurgery Study Group

Abstract: PURPOSE: To better predict permanent complications from arteriovenous malformation (AVM) radiosurgery. METHODS AND MATERIALS: Data from 85 AVM patients who developed symptomatic complications following gamma knife radiosurgery and 337 control patients with no complications were evaluated as part of a multi-institutional study. Of the 85 patients with complications, 38 patients were classified as having permanent symptomatic sequelae (necrosis). AVM marginal doses varied from 10-35 Gy and treatment volumes from 0.26-47.9 cc. Median follow-up for patients without complications was 45 months (range: 24-92). RESULTS: Multivariate analysis of the effects of AVM location and the volume of tissue receiving 12 Gy or more (12-Gy-Volume) allowed construction of a significant postradiosurgery injury expression (SPIE) score. AVM locations in order of increasing risk and SPIE score (from 0-10) were: frontal, temporal, intraventricular, parietal, cerebellar, corpus callosum, occipital, medulla, thalamus, basal ganglia, and pons /midbrain. The final statistical model predicts risks of permanent symptomatic sequelae from SPIE scores and 12-Gy-Volumes. Prior hemorrhage, marginal dose, and Marginal-12-Gy-Volume (target volume excluded) did not significantly improve the risk-prediction model for permanent sequelae ($p \geq 0.39$). CONCLUSION: The risks of developing permanent symptomatic sequelae from AVM radiosurgery vary dramatically with location and, to a lesser extent, volume. These risks can be predicted according to the SPIE location-risk score and the 12-Gy- Volume.

50.

Year: 2000

Patient number: 422

Author: Flickinger, John C.; Kondziolka, Douglas; Lunsford, L. Dade; Kassam, Amin; Phuong, Loi K.; Liscak, Roman; Pollock, Bruce

Reference: International Journal of Radiation Oncology Biology Physics, 46, 5, 1143-1148, 2000

Title: Development of a model to predict permanent symptomatic postradiosurgery injury for arteriovenous malformation patients

Abstract: Purpose: To better predict permanent complications from arteriovenous malformation (AVM) radiosurgery. Methods and Materials: Data from 85 AVM patients who developed symptomatic complications following gamma knife radiosurgery and 337 control patients with no complications were evaluated as part of a multi-institutional study. Of the 85 patients with complications, 38 patients were classified as having permanent

symptomatic sequelae (necrosis). AVM marginal doses varied from 10-35 Gy and treatment volumes from 0.26-47.9 cc. Median follow-up for patients without complications was 45 months (range: 24-92). Results: Multivariate analysis of the effects of AVM location and the volume of tissue receiving 12 Gy or more (12-Gy-Volume) allowed construction of a significant postradiosurgery injury expression (SPIE) score. AVM locations in order of increasing risk and SPIE score (from 0-10) were: frontal, temporal, intraventricular, parietal, cerebellar, corpus callosum, occipital, medulla, thalamus, basal ganglia, and pons /midbrain. The final statistical model predicts risks of permanent symptomatic sequelae from SPIE scores and 12-Gy-Volumes. Prior hemorrhage, marginal dose, and Marginal-12-Gy-Volume (target volume excluded) did not significantly improve the risk-prediction model for permanent sequelae ($p \geq 0.39$). Conclusion: The risks of developing permanent symptomatic sequelae from AVM radiosurgery vary dramatically with location and, to a lesser extent, volume. These risks can be predicted according to the SPIE location-risk score and the 12-Gy-Volume.

51.

Year: 2000

Patient number: 208

Author: Huh, S. K.; Lee, K. C.; Lee, K. S.; Kim, D. I.; Park, Y. G.; Chung, S. S.

Reference: Journal of clinical neuroscience, 7, 5, 429-33, 2000

Title: Selection of treatment modalities for cerebral arteriovenous malformations: a retrospective analysis of 348 consecutive cases

Abstract: The objective was to establish the selection criteria for the optimal management modalities for cerebral arteriovenous malformations. We analysed the complications and late outcomes in 348 consecutive cases (132 microsurgical resections, 202 stereotactic radiosurgeries, 8 embolisations only, 6 combined treatments) managed at Yonsei University Hospital from 1988 to 1997. Files for all patients were analysed. The outcome was classified into good for the patients who returned to their previous job with or without neurological deficits, fair for the patients who were unable to return to work but performed daily activities independently with minor deficits, and poor for the patients who were performing dependent daily activities with major deficits. The outcome of microsurgery was considered good in 108 patients (81.8%), fair in 18 (13.6%), poor in 4 (3.1%), and 2 (1.5%) patients died. Initial insults and haemodynamic complications were the major cause of an unfavourable outcome. The cumulative occlusion rate of the nidus after radiosurgery was 10.2% within 12 months, 75.3% within 24 months, and 89.8% within 36 months. Perilesional imaging changes with neurological deficits (4 permanent and 6 transient, 4.8%) and haemorrhage (16 patients, 7.7%) during the latent interval were the major cause of an unfavourable outcome (1 poor, 4 dead after radiosurgery). Postradiosurgery bleeding occurred frequently within 6 months (6 patients), and between 13 and 24 months (8 patients). In conclusion, selection of treatment modality for cerebral AVMs depends on the preoperative evaluation of the risk/benefit ratio in each case. Microsurgical removal, which eliminates the risk of bleeding immediately, is preferred for lesions in non-eloquent areas. Radiosurgery is an effective treatment modality for small lesions in eloquent areas, but has a substantial risk of haemorrhage during the latency

period. Results of this study suggest that microsurgical removal should be considered for lesions in eloquent areas with high haemorrhage risk, such as prior haemorrhage, medium to large size lesion, and single deep venous drainage. Copyright 2000 Harcourt Publishers Ltd.

52.

Year: 2000

Patient number: 79

Author: Kida, Y.; Kobayashi, T.; Tanaka, T.; Mori, Y.; Hasegawa, T.; Kondoh, T.

Reference: Journal of clinical neuroscience, 7, Suppl 1, 6-9, 2000

Title: Seizure control after radiosurgery on cerebral arteriovenous malformations

Abstract: Among 462 cases of cerebral arteriovenous malformation (AVM) treated with gamma-radiosurgery, the initial presentations were haemorrhage in 68%, epilepsy in 12.8%, neurological deficits in 3.2%, minor symptoms in 7.6% and asymptomatic in 4.5% respectively. There were 79 cases (17.1%) who had had a convulsive seizure before radiosurgery and they were classified into two groups: 58 cases presented with seizure as an initial symptoms (group A) and the other 21 cases mostly had seizures following intracranial haemorrhage (group B). Before radiosurgery, generalised seizure was the predominant seizure pattern in both groups, followed by pure partial and complex partial seizures. There was no major difference in seizure patterns or seizure frequency in group A and B. At radiosurgery AVMs were treated with a mean maximum dose of 37.2 Gy and a marginal dose of 19.8 Gy. Seizures had apparently decreased in most of the cases at the last follow-up (mean 24 months) according to the obliteration of the nidus. Seizures were either decreased or had disappeared in 91.6% of group A and 62.5% of group B patients. The overall results indicate that seizures improved in 85.5%, were changed in 11.6% and deteriorated in 2.9% of patients. Radiosurgery is effective not only for the obliteration of nidus of cerebral AVM, but also for seizure control, even before complete occlusion of the nidus.

53.

Year: 2000

Patient number: 30

Author: Kurita, H.; Kawamoto, S.; Sasaki, T.; Shin, M.; Tago, M.; Terahara, A.; Ueki, K.; Kirino, T.

Reference: Journal of neurology neurosurgery and psychiatry, 68, 5, 563-70, 2000

Title: Results of radiosurgery for brain stem arteriovenous malformations

Abstract: **OBJECTIVE:** To assess the treatment results of radiosurgery for brain stem arteriovenous malformations (AVMs) and to seek optimal dose and treatment volume prescription for these lesions. **METHODS:** The clinical and radiological data of 30 consecutive patients with brain stem AVM treated with gamma knife radiosurgery were retrospectively reviewed with a mean follow up period of 52.2 months. There were 26 patients with previous haemorrhages and 21 with neurological deficit. Seventeen AVMs

were located in the midbrain, 11 in the pons, and two in the medulla oblongata. All of the lesions were small with the intra-axial component occupying less than one third of the area of brain stem parenchyma on axial section of multiplanar MRI or CT. The mean diameter of the nidus was 1.26 cm, and the nidus volume within the brain stem parenchyma ranged from 0.1 to 2.0 cm³. The mean radiation dose to the AVM margin was 18.4 Gy. RESULTS: The actuarial 3 year obliteration rate was 52.2%; 69.4% in cases treated with standard doses (minimum target dose, 18-20Gy), and 14.3% in cases treated with low doses (<18 Gy) (p<0.05). Two patients sustained symptomatic radiation injury, but there was no permanent neurological deficit caused by radiosurgery. Five patients had haemorrhage from the AVM after irradiation, including four fatal cases, resulting in a 4.0% annual rate of post-treatment bleeding. CONCLUSIONS: Radiosurgery is a viable treatment modality for patients with small deep parenchymal brain stem AVMs. A standard radiosurgical dose is safe and effective when directed to a small treatment volume. However, latent interval haemorrhage remains a significant problem until the nidus is obliterated completely.

54.

Year: 2000

Patient number: 36

Author: Kurita, H.; Ueki, K.; Shin, M.; Kawamoto, S.; Sasaki, T.; Tago, M.; Kirino, T.

Reference: Journal of neurosurgery, 93, 2, 224-8, 2000

Title: Headaches in patients with radiosurgically treated occipital arteriovenous malformations

Abstract:OBJECT: The goal of this study was to determine the prevalence, characteristics, and radiosurgical outcomes of headaches associated with occipital arteriovenous malformations (AVMs). METHODS: The authors reviewed the medical records of 37 consecutive patients with occipital AVMs who had been treated by radiosurgery to identify the radiological features of the AVMs before and after treatment and the clinical features and outcomes of headaches described in accordance with the criteria of the International Headache Society (IHS). Thirty-six patients (97.3%) were followed for a mean period of 46.6 months. The median volume of the AVMs was 1.9 cm³, to which a mean radiation dose of 21.6 Gy was delivered. In the entire study group, periodic headaches were found in 17 patients (45.9%), of whom seven (18.9%) suffered from migraines with the characteristic visual aura. Migraine was predominantly found in patients with right-sided (p = 0.038) or laterally located (p = 0.025) AVMs. Factors associated with a higher incidence of any type of headache included larger nidus volume (p = 0.02), tortuous change of feeding artery (p = 0.036), and cortical drainage with reflux in the superior sagittal sinus (p = 0.032). The actuarial rate of angiographic obliteration was 71.6% at 3 years. Headaches resolved or improved in 12 (70.6%) of 17 patients, including six (85.7%) of seven with migraine. The outcome of headache closely correlated with the obliteration results of the AVM (p = 0.002). CONCLUSIONS: A portion of occipital AVMs do cause headaches that satisfy the current IHS criteria for migraine, and the prevalence varies by the topography of the lesion. Radiosurgery can resolve headaches in the majority of treated patients.

55.

Year: 2000

Patient number: 123

Author: Kwon, Y.; Jeon, S. R.; Kim, J. H.; Lee, J. K.; Ra, D. S.; Lee, D. J.; Kwun, B. D.

Reference: Journal of neurosurgery, 93, Suppl 3, 104-6, 2000

Title: Analysis of the causes of treatment failure in gamma knife radiosurgery for intracranial arteriovenous malformations

Abstract:OBJECT: The authors sought to analyze causes for treatment failure following gamma knife radiosurgery (GKS) for intracranial arteriovenous malformations (AVMs), in cases in which the nidus could still be observed on angiography 3 years postsurgery. METHODS: Four hundred fifteen patients with AVMs were treated with GKS between April 1990 and March 2000. The mean margin dose was 23.6 Gy (range 10-25 Gy) , and the mean nidus volume was 5.3 cm³ (range 0.4-41.7 cm³). The KULA treatment planning system and conventional subtraction angiography were used in treatment planning. One hundred twenty-three of these 415 patients underwent follow-up angiography after GKS. After 3 years the nidus was totally obliterated in 98 patients (80%) and partial obliteration was noted in the remaining 25. There were several reasons why complete obliteration was not achieved in all cases: inadequate nidus definition in four patients, changes in the size and location of the nidus in five patients due to recanalization after embolization or reexpansion after hematoma reabsorption, a large AVM volume in five patients, a suboptimal radiation dose to the thalamic and basal ganglia in eight patients, and radioresistance in three patients with an intranidal fistula. CONCLUSIONS: The causes of failed GKS for treatment of AVMs seen on 3-year follow-up angiograms include inadequate nidus definition, large nidus volume, suboptimal radiation dose, recanalization/reexpansion, and radioresistance associated with an intranidal fistula.

56.

Year: 2000

Patient number: 53

Author: Levy, E. I.; Niranjana, A.; Thompson, T. P.; Scarrow, A. M.; Kondziolka, D.; Flickinger, J. C.; Lunsford, L. D.; Breeze, R. E.; Friedman, W. A.; Gutin, P. H.; Loeffler, J. S.

Reference: Neurosurgery, 47, 4, 834-842, 2000

Title: Radiosurgery for childhood intracranial arteriovenous malformations

Abstract:OBJECTIVE: The optimal management of intracranial arteriovenous malformations (AVMs) in children remains controversial. Children with intracranial AVMs present a special challenge in therapeutic decision-making because of the early recognition of their future life-long risks of hemorrhage if they are treated conservatively. The goals of radiosurgery are to achieve complete AVM obliteration and to preserve neurological function. We present long-term outcomes for a series of children treated using radiosurgery. METHODS: The findings for 53 consecutive children who underwent

at least 36 months of imaging follow-up monitoring after radiosurgery were reviewed. The median age at the time of treatment was 12 years (range, 2-17 yr). Thirty-one children (58%) presented after their first intracranial hemorrhaging episodes, two (4%) after their second hemorrhaging episodes, and one (2%) after five hemorrhaging episodes. Nineteen children (36%) presented with unruptured AVMs, and a total of 25 children (47%) exhibited neurological deficits. AVMs were graded as Spetzler-Martin Grade I (2%), Grade II (23%), Grade III (36%), Grade IV (9%), or Grade

57.

Year: 2000

Patient number: 48

Author: Lindqvist, M.; Karlsson, B.; Guo, W. Y.; Kihlström, L.; Lippitz, B.; Yamamoto, M.

Reference: Neurosurgery, 46, 4, 803-8, 2000

Title: Angiographic long-term follow-up data for arteriovenous malformations previously proven to be obliterated after gamma knife radiosurgery

Abstract:OBJECTIVE: To investigate whether angiograms obtained 2 years after radiosurgery, proving total arteriovenous malformation (AVM) occlusion, represent the final state of treated AVMs and adjacent normal vessels. METHODS: Angiograms were obtained for 48 patients 5 to 24 years after gamma knife radiosurgery and 4 to 17 years after the AVMs had been proven to be totally occluded after the treatment; changes in normal vessels and signs of recanalization were recorded. Ten of the patients developed clinical symptoms attributable to the AVMs or the treatment after having been declared cured, whereas the other patients did not exhibit symptoms. RESULTS: There was evidence of AVM nidi at the sites of previously occluded AVMs for two patients and of nidi adjacent to those sites for another two patients. Three of the four recurrent AVMs were associated with hemorrhaging. All patients who experienced hemorrhaging from previously occluded AVMs were \leq 14 years of age at the time of gamma knife radiosurgery. There were signs of segmental narrowing in normal vessels that had been irradiated with high doses (nine patients) or a low dose (one patient). The segmental narrowing decreased with time for four of these patients, was unchanged for four, and increased for two. These vascular changes did not produce clinical symptoms in any of the patients. CONCLUSION: There is a small possibility that AVMs may reappear after having been totally occluded after radiosurgery, especially in pediatric patients. Segmental narrowing in normal arteries after radiosurgery is a benign condition that rarely progresses and does not produce clinical symptoms.

58.

Year: 2000

Patient number: 41

Author: Maesawa, S.; Flickinger, J. C.; Kondziolka, D.; Lunsford, L. D.

Reference: Journal of neurosurgery, 92, 6, 961-70, 2000

Title: Repeated radiosurgery for incompletely obliterated arteriovenous malformations

Abstract:OBJECT: The goal of this study was to define treatment results of repeated arteriovenous malformation (AVM) radiosurgery, namely AVM obliteration and complications. METHODS: The authors analyzed their experience with repeated AVM radiosurgery performed in 41 patients for whom follow-up review lasted at least 2 years. The median duration of follow up was 34 months (range 7-65 months) after repeated radiosurgery in this group. The residual nidus was located within the area of focus (in field) of the initial radiosurgery in 28 patients (68%). Initial doses to the margin varied from 12.5 to 20 Gy (median 18 Gy). During repeated treatment the dose to the margin varied from 12.5 to 20 Gy (median 17 Gy) and the retreated volumes ranged from 0.4 to 7 cm³ (median 2.1 cm³). Follow-up angiography performed at least 2 years postradiosurgery revealed complete AVM obliteration in 21 (70%) of 30 patients. The estimated overall 2-year obliteration rate, based on findings on magnetic resonance imaging (eight of 11 obliterated) and angiography (29 of 41 obliterated) was 71%. Obliteration rates correlated with margin doses ($p = 0.0045$) with a trend toward higher rates in cases with in-field nidus persistence ($p = 0.0637$). The dose- response curve for AVM nidus obliteration was not significantly different from that of the initial radiosurgery. In two patients (5%) intracranial AVM hemorrhage developed within 125.9 risk years after repeated radiosurgery (1.6% per patient year). Persistent symptomatic adverse radiation effects developed in two (5%) of 41 patients following repeated radiosurgery. Postradiosurgical imaging changes were identified in 11 (27%) of 41 patients, which correlated with a 12-Gy volume from repeated surgery ($p = 0.019$). CONCLUSIONS: When necessary, repeated AVM radiosurgery achieves obliteration with an acceptable risk. Despite the effects of previous irradiation, repeated radiosurgery required similar or slightly higher radiation doses to achieve the same in-field obliteration rates as those needed to obliterate an AVM that had not been treated by radiation previously.

59.

Year: 2000

Patient number: 87

Author: Massager, N.; Régis, J.; Kondziolka, D.; Njee, T.; Levivier, M.

Reference: Journal of neurosurgery, 93, Suppl 3, 102-3, 2000

Title: Gamma knife radiosurgery for brainstem arteriovenous malformations: preliminary results

Abstract:OBJECT: This study was undertaken to assess the efficacy and safety of gamma knife radiosurgery (GKS) for the treatment of arteriovenous malformations (AVMs) located within the brainstem. METHODS: The results of GKS performed in 87 patients with brainstem AVMs at two centers with experienced physicians are reviewed. The mean patient age was 37 years and the population included 19 children. The male/female ratio was 56:31. The malformation was located in the upper brainstem in 52 patients. Seventy-four percent of the patients had suffered a hemorrhage before GKS. For 70% of the patients no other treatment had been proposed before GKS. The mean AVM volume was 1.3 cm³. The lesions were treated with one to eight isocenters, with a margin dose ranging between 11.5 Gy and 30 Gy. The mean clinical follow-up period was 3.2 years. Ninety-five percent of the patients improved or remained neurologically stable.

Rebleeding occurred in three patients at 3, 6, and 16 months, respectively, after GKS. Two patients in whom rebleeding occurred recovered, and one died. The AVM obliteration rate was 63% at 2 years and 73% at 3 years after GKS. A second GKS was performed in six patients in whom only partial obliteration was demonstrated on angiography 3 years after the first procedure. **CONCLUSIONS:** Gamma knife radiosurgery may be a valuable first-choice therapy for the treatment of AVMs located within the brainstem.

60.

Year: 2000

Patient number: 37

Author: Miyachi, S.; Negoro, M.; Okamoto, T.; Kobayashi, T.; Kida, Y.; Tanaka, T.; Yoshida, J.

Reference: Journal of clinical neuroscience, 7, Suppl 1, 82-5, 2000

Title: Embolisation of cerebral arteriovenous malformations to assure successful subsequent radiosurgery

Abstract: This study investigated the angiographic changes in embolised arteriovenous malformations (AVMs) pre- and post-embolisation and preradiosurgery to clarify the usefulness of embolisation as a pretreatment for radiosurgery and the strategy of embolisation for the radiosurgical success. A total of 37 patients with cerebral AVMs treated over a period of 4 years was investigated. All the AVMs were embolised with N-butyl cyanoacrylate and 2 months later they were treated by radiosurgery. The size of AVM nidus reduced just following the embolisation (mean 21.9 ml to 3.9 ml). The angiogram taken in preparation for radiosurgery showed a further size reduction in the nidus of 16 AVMs, no change in 10 and regrowth in 11. In all the cases where size was reduced, the nidus was densely packed, while all the regrown AVMs were of the diffuse type. Five AVMs disappeared following radiosurgery, all of which were size-reduction or no-change cases. In conclusion, to achieve success in subsequent radiosurgery, nidus embolisation and the occlusion of fistulous and meningeal feeders are mandatory. Imprudent proximal feeder occlusion and the use of embolic materials with a risk of recanalisation should be avoided to prevent regrowth of the nidus, which may lead to errors in planning the radiosurgery to follow.

61.

Year: 2000

Patient number: 76

Author: Pan, D. H.; Guo, W. Y.; Chung, W. Y.; Shiao, C. Y.; Chang, Y. C.; Wang, L. W.

Reference: Journal of neurosurgery, 93, Suppl 3, 113-9, 2000

Title: Gamma knife radiosurgery as a single treatment modality for large cerebral arteriovenous malformations

Abstract: OBJECT: A consecutive series of 240 patients with arteriovenous malformations (AVMs) treated by gamma knife radiosurgery (GKS) between March 1993 and March 1999 was evaluated to assess the efficacy and safety of radiosurgery for

cerebral AVMs larger than 10 cm³ in volume. **METHODS:** Seventy-six patients (32%) had AVM nidus volumes of more than 10 cm³. During radiosurgery, targeting and delineation of AVM nidi were based on integrated stereotactic magnetic resonance (MR) imaging and x-ray angiography. The radiation treatment was performed using multiple small isocenters to improve conformity of the treatment volume. The mean dose inside the nidus was kept between 20 Gy and 24 Gy. The margin dose ranged between 15 to 18 Gy placed at the 55 to 60% isodose centers. Follow up ranged from 12 to 73 months. There was complete obliteration in 24 patients with an AVM volume of more than 10 cm³ and in 91 patients with an AVM volume of less than 10 cm³. The latency for complete obliteration in larger-volume AVMs was significantly longer. In Kaplan-Meier analysis, the complete obliteration rate in 40 months was 77% in AVMs with volumes between 10 to 15 cm³, as compared with 25% for AVMs with a volume of more than 15 cm³. In the latter, the obliteration rate had increased to 58% at 50 months. The follow-up MR images revealed that large-volume AVMs had higher incidences of postradiosurgical edema, petechiae, and hemorrhage. The bleeding rate before cure was 9.2% (seven of 76) for AVMs with a volume exceeding 10 cm³, and 1.8% (three of 164) for AVMs with a volume less than 10 cm³. Although focal edema was more frequently found in large AVMs, most of the cases were reversible. Permanent neurological complications were found in 3.9% (three of 76) of the patients with an AVM volume of more than 10 cm³, 3.8% (three of 80) of those with AVM volume of 3 to 10 cm³, and 2.4% (two of 84) of those with an AVM volume less than 3 cm³. These differences in complications rate were not significant. **CONCLUSIONS:** Recent improvement of radiosurgery in conjunction with stereotactic MR targeting and multiplanar dose planning has permitted the treatment of larger AVMs. It is suggested that gamma knife radiosurgery is effective for treating AVMs as large as 30 cm³ in volume with an acceptable risk.

62.

Year: 2000

Patient number: 10

Author: Pollock, B. E.; Kline, R. W.; Stafford, S. L.; Foote, R. L.; Schomberg, P. J.

Reference: International Journal of Radiation Oncology Biology Physics, 48, 3, 817-824, 2000

Title: The rationale and technique of staged-volume arteriovenous malformation radiosurgery

Abstract: Purpose: Stereotactic radiosurgery is an effective management strategy for properly selected arteriovenous malformation (AVM) patients. However, the risk of postradiosurgical radiation-related injury generally limits this procedure to patients with AVMs of an average diameter of 3 cm or less. Radiosurgery of large AVMs in a planned staged fashion was undertaken to limit the radiation exposure to the surrounding normal brain. Methods and Materials: Between April 1997 and December 1999, 10 patients with a median AVM volume of 17.4 cm³ (range, 7.4-53.3 cm³) underwent staged-volume radiosurgery (23 procedures). At the first radiosurgical procedure, the total volume of the AVM is estimated and a dose plan calculated that covers 10 cm³-15 cm³, or one-half the nidus volume if the AVM is critically located (brainstem, thalamus, or basal ganglia). At

6-month intervals thereafter, radiosurgery was repeated to different portions of the AVM with the previous dose plan(s) being re-created utilizing intracranial landmarks to minimize radiation overlap. Radiosurgical procedures were continued until the entire malformation has been irradiated. Results: The radiation dosimetry of staged- volume AVM radiosurgery was compared to hypothetical single-session procedures for the 10 patients. Staged-volume radiosurgery decreased the 12- Gy volume by an average of 11.1% (range, 4.9-21%) ($p < 0.001$). The non-AVM 12-Gy volume was reduced by an average of 27.2% (range, 12.5-51.3%) ($p < 0.001$). Discussion: Staged-volume radiosurgery of large AVMs results in less radiation exposure to the adjacent brain. Further follow-up is needed to determine whether this technique provides a high rate of AVM obliteration while maintaining an acceptable rate of radiation-related complications. (C) 2000 Elsevier Science Inc.

63.

Year: 2000

Patient number: 150

Author: Unger, F.; Papaefthymiou, G.; Eustacchio, S.; Trummer, M.; Pendl, G.

Reference: Acta Chirurgica Austriaca, 32, 5, 233-235, 2000

Title: Hydrocephalus - A major complication after stereotactic radiosurgical gamma knife treatment?

Abstract:Background: Hydrocephalus formation following Gamma Knife radiosurgery has been repeatedly reported in the literature. Experiences in patients treated at our own institution are presented here. Methods: 1500 patients underwent stereotactic radiosurgery with the Gamma Knife at the Department of Neurosurgery at the Karl Franzens University in Graz from April 1992 until January 1999 (age ranging from 2 to 88 years, median 51). Single dose radiosurgery was performed with use of a Gamma Unit (Modell B, 201 Cobalt-60 bears). Among those patients were 333 with meningioma, 277 with metastases, 189 had glial tumors, 186 acoustic neurinoma and 150 arteriovenous malformations. Clinical and neuroradiological follow-up examinations were performed every six months, in patients with malignant tumors at intervals of 3 months. Results: 33 patients had a preexistent hydrocephalus 20 of whom had been treated surgically with tumor resection prior to Gamma Knife treatment, in all patients ventriculoperitoneal shunts had to be inserted radiosurgery. After radiosurgery 3 patients with acoustic neurinomas and initially normal ventricular system developed hydrocephalus. Microsurgical tumor debulking was performed in two cases. The third patient was treated by means of a ventriculoperitoneal shunt. Conclusions: Tumor-associated hydrocephalus with predictable course was observed in 2 % of all patients. By contrast, treatment-related peritumoral reaction sufficient to block the CSF circulation and requiring shunt insertion was observed only in 0.2 % of all patients and concerned less than 2 % patients with acoustic neurinomas. The aim of radiosurgery in tumor patients is growth control. In cases with preexisting aquaeductal obstruction occlusive hydrocephalus may develop especially in the phase of radiogenic perifocal edema. This fact should be discussed with patients who are not operated due to medical problems or who refuse surgery. Patients having undergone a shunting procedure already before radiosurgery are likely to remain

shunt-dependent. Hydrocephalus formation is not a typical complication but is a symptom that may aggravate after radiosurgery.

64.

Year: 1999

Patient number: 10

Author: Blonder, L. X.; Hodes, J. E.; Ranseen, J. D.; Schmitt, F. A.

Reference: Applied neuropsychology, 6, 3, 181-6, 1999

Title: Short-term neuropsychological outcome following Gamma Knife radiosurgery for arteriovenous malformations: a preliminary report

Abstract: This study investigated the effect of Gamma Knife radiosurgery for the treatment of arteriovenous malformations (AVMs) on neuropsychological functioning. We examined neuropsychological performance in 10 patients before and after radiosurgical treatment with the Leksell cobalt-60 Gamma Knife unit. The patients included 7 right-handed women and 3 right-handed men. Three patients had left hemisphere AVMs, 4 had right hemisphere AVMs, and 3 had midline AVMs. Each patient was given neuropsychological testing within 1 week before Gamma Knife radiosurgery. Testing was repeated an average of 11.4 months after treatment. There were no statistically significant differences between pre- and postradiosurgical neuropsychological test scores on any measure. Pretreatment AVM diameter as measured on magnetic resonance scans ranged from 1.6 to 6.5 cm. After treatment, 2 AVMs disappeared, 4 decreased slightly in size, and 4 remained unchanged. We conclude that Gamma Knife radiotherapy in this sample of patients was neither detrimental nor beneficial to neuropsychological functioning.

65.

Year: 1999

Patient number: 102

Author: Flickinger, J. C.; Kondziolka, D.; Lunsford, L. D.; Pollock, B. E.; Yamamoto, M.; Gorman, D. A.; Schomberg, P. J.; Sneed, P.; Larson, D.; Smith, V.; McDermott, M. W.; Miyawaki, L.; Chilton, J.; Morantz, R. A.; Young, B.; Jokura, H.; Liscak, R.

Reference: International journal of radiation oncology biology physics, 44, 1, 67-74, 1999

Title: A multi-institutional analysis of complication outcomes after arteriovenous malformation radiosurgery

Abstract: **PURPOSE:** To better understand radiation complications of arteriovenous malformation (AVM) radiosurgery and factors affecting their resolution. **METHODS AND MATERIALS:** AVM patients (102/1255) who developed neurological sequelae after radiosurgery were studied. The median AVM marginal dose (D_{min}) was 19 Gy (range: 10-35). The median volume was 5.7 cc (range: 0.26-143). Median follow-up was 34 months (range: 9-140). **RESULTS:** Complications consisted of 80/102 patients with evidence of radiation injury to the brain parenchyma (7 also with cranial nerve deficits, 12 also with seizures, 5 with cyst formation), 12/102 patients with isolated cranial

neuropathies, and 10/102 patients with only new or worsened seizures. Severity was classified as minimal in 39 patients, mild in 40, disabling in 21, and fatal in 2 patients. Symptoms resolved completely in 42 patients for an actuarial resolution rate of 54% +/- 7% at 3 years post-onset. Multivariate analysis identified significantly greater symptom resolution in patients with no prior history of hemorrhage ($p = 0.01$, 66% vs. 41%), and in patients with symptoms of minimal severity: headache or seizure as the only sequelae of radiosurgery ($p < 0.0001$, 88% vs. 34%). **CONCLUSION:** Late sequelae of radiosurgery manifest in varied ways. Further long-term studies of these problems are needed that take into account symptom severity and prior hemorrhage history.

66.

Year: 1999

Patient number: 38

Author: Guo, W. Y.; Pan, H. C.; Shiau, C. Y.; Chang, Y. C.; Wu, H. M.; Chung, W. Y.; Wang, L. W.; Teng, M. M. H.

Reference: Rivista di Neuroradiologia, 12, SUPPL. 2, 35-40, 1999

Title: AVM radiosurgery: Where is the volume limit?

Abstract: To evaluate the role of radiosurgery for large AVM (nidus volume > 8 ml). 200 cerebral AVM patients treated by Gamma Knife radiosurgery constituted the study database. Of them, 90 had a nidus volume > 8 ml. 38 of the 90 patients who fulfilled the following criteria were enrolled in result analysis. They were either treated more than 24 months ago or proved cured at any time earlier than 24 months. Grades of the AVM were II/2, III/11, IV/20, V/5 (Spetzler-Martin grading system). Integrated stereotaxic MR and stereotaxic x-ray angiography were used for treatment guidance. Volumes of the AVM nidi of the 38 patients were 8-26 ml, median 11 ml. The prescribed mean maximum and minimum irradiation doses to the delineated AVM nidi were 36 Gy and 18 Gy, respectively. 21 patients were cured of AVM at 18-36, mean 23 months, after radiosurgery. Almost complete obliteration occurred in 6 patients at 24-46, mean 37 months, and subtotal obliteration occurred in 11 patients at 27-60, mean 38 months, after radiosurgery. Nidus volume, not AVM grading, had an impact on the cure rate of AVM radiosurgery. T2-weighted high signals in the vicinity of the AVM were observed in 32 of 38 patients. Minor neurological deficits occurred in 3 patients. Re-bleeding occurred in 3 patients during the follow-up periods. Gamma Knife radiosurgery is currently an effective treatment alternative for large AVM, up to a nidus volume of 21 ml. The waiting time for complete obliteration of large AVM appears to be longer than for small ones. Nidus volume is the most decisive factor in radiosurgery of large AVM. Application of MR improves the conformity of treatment volume in AVM radiosurgery. The improvement minimizes the irradiation volumes and makes radiosurgery for large AVM safer.

67.

Year: 1999

Patient number: 213

Author: Inoue, H. K.; Nagaseki, Y.; Naitou, I.; Negishi, M.; Hirato, M.; Shibasaki, T.; Ohye,

C.; Andou, Y.

Reference: *Interventional Neuroradiology*, 5, SUPPL. 1, 171-176, 1999

Title: The role of intravascular embolization prior to radiosurgery of cerebral arteriovenous malformations

Abstract: The role of intravascular embolization prior to radiosurgery of cerebral arteriovenous malformations was evaluated based on the basis of the results of gamma knife radiosurgery in relation to hemorrhage and early obliteration after treatment. Nine of 213 patients experienced hemorrhage 4 to 42 months after radiosurgery. All AVMs in these patients had dilated feeding arteries, and the flow of the AVM was rapid and/or high. An intranidal aneurysm was seen in one patient. Drainage of all AVMs consisted of a single and/or deep draining veins, and venous obstruction was found in six. Sixty-three of 87 patients followed for more than four years after radiosurgery were examined angiographically, and total obliteration of AVM was observed in 52 of them (82.5%). Early obliteration was found in 19 of the 34 patients examined within 12 months. The obliteration rate was significantly higher in slow- and low-flow AVMs (73.9%) than in rapid- and/or high- flow AVMs (18.2%). It is concluded that the role of intravascular embolization prior to radiosurgery is not only decreasing the size of the AVM but decreasing the risk of hemorrhage and shortening the latency period by decreasing their flow rate and flow volume.

68.

Year: 1999

Patient number: 838

Author: Karlsson, B.; Lax, I.; Söderman, M.

Reference: *International journal of radiation oncology biology physics*, 43, 2, 313-9, 1999

Title: Can the probability for obliteration after radiosurgery for arteriovenous malformations be accurately predicted?

Abstract: **PURPOSE:** To investigate how accurate different models predict the probability for obliteration following radiosurgery for an arteriovenous malformation (AVM). **METHODS AND MATERIALS:** The probability for obliteration was calculated for all 838 AVMs with a known treatment outcome and treated at the Karolinska Hospital with Gamma Knife surgery 1970-1993. Four different models were used for the calculation, resulting in four different values of the probability for obliteration. The calculated prediction values were added for each model, and the total number of predicted obliteration compared to that observed in the whole patient material as well as in different subgroups. **RESULTS:** Three of the four models predicted the total number of obliterations accurately. In two of those three models, the accuracy of the prediction was dependent on AVM volume and treatment dose. In one model only, the prediction was accurate and independent of all investigated parameters. **CONCLUSIONS:** The probability for obliteration was accurately predicted by one of the models analyzed. In this model, the probability for obliteration was related to the dose to the AVM periphery only. The AVM volume had no independent impact on the probability for obliteration. There was a trend that AVMs with a central location had a better obliteration rate than predicted.

69.

Year: 1999

Patient number: NA abstract

Author: Negoro, M.; Miyachi, S.; Hattori, T.; Okamoto, T.; Fukui, K.; Fukasaku, K. A.; Iwakoshi, T.; Yoshida, J.

Reference: Interventional Neuroradiology, 5, SUPPL. 1, 167-170, 1999

Title: The selection and result of AVM treatment

Abstract: The treatment selection for cerebral arteriovenous malformation (AVM) still is in controversy. In order to find out the best way to treat AVM, we summarized the treatment result of AVM patients in our hospital. Sixty-three AVM patients who had been treated at Nagoya University Hospital since 1988 to 1997 were studied. The patient characteristics were nearly the same as other reported series. The treatment modalities include surgery, embolization and radiosurgery. Rate of nidus disappearance was assessed in each treatment. Highest rate was observed in surgery or surgery with embolization. But new neurological deficits were seen in 37% of the patients of same group. Nidus occlusion rate was not high in radiosurgery with embolization, but low in complication rate. The result showed the importance of embolization procedure in the treatment selection of AVM. The value of functional MRI as pre-therapeutic study is high in those patients whose AVM adjacent to eloquent area.

70.

Year: 1999

Patient number: 97

Author: Pollock, B. E.; Gorman, D. A.; Schomberg, P. J.; Kline, R. W.

Reference: Mayo Clinic proceedings, 74, 1, 5-13, 1999

Title: The Mayo Clinic gamma knife experience: indications and initial results

Abstract: **OBJECTIVE:** To review the results and expectations of contemporary stereotactic radiosurgery. **MATERIAL AND METHODS:** We conducted a retrospective analysis of 1,033 consecutive patients who underwent gamma knife radiosurgery at Mayo Clinic Rochester between January 1990 and January 1998. **RESULTS:** The number of patients undergoing radiosurgery increased from 57 in 1990 to 216 in 1997. Of 97 patients with arteriovenous malformations who underwent follow-up angiography 2 years or more after a single radiosurgical procedure, 72 (74%) had complete obliteration of the vascular malformation. Of 209 patients who underwent radiosurgery for benign tumors (schwannomas, meningiomas, or pituitary adenomas) and had radiologic studies after 2 years or more of follow-up, tumor growth control was noted in 200 (96%). Tumor growth was also controlled in 90% of brain metastatic lesions at a median of 7 months after radiosurgery. Of 20 patients with trigeminal neuralgia and follow-up for more than 2 months, 14 (70%) were free of pain after radiosurgery. **CONCLUSION:** Radiosurgery is a safe and effective management strategy for a wide variety of intracranial disorders. Use of radiosurgical treatment should continue to increase as more data become available on

the long-term results of this procedure.

71.

Year: 1999

Patient number: 41

Author: Vymazal, J.; Liscák, R.; Novotný³, J., Jr.; Janousková, L.; Vladyka, V.

Reference: Stereotactic and functional neurosurgery, 72, Suppl 1, 175-84, 1999

Title: The role of Gamma Knife radiosurgery in arteriovenous malformation with aneurysms

Abstract: A review of 217 patients treated with Gamma knife radiosurgery (GKRS), at Hospital Na Homolce, Prague, between October 1992 and January 1998 for arteriovenous malformation (AVM) is presented. Forty-one patients (18.9%) with an AVM and associated aneurysm are the subjects of special interest for this study. The nidus volume in the presence of an aneurysm lying close to the nidus or within it was significantly larger than the nidus volume in cases where the AVMs had no associated aneurysm, suggesting that an increased flow in a larger AVM may be an important factor for aneurysm formation. The association of an arterial aneurysm with an AVM significantly increased the chance of hemorrhage when compared to the group with AVM and no aneurysm. Ten patients out of 14, who had an aneurysm close to or within the nidus, showed a complete obliteration of their AVM and aneurysm, although the latter was not always included within the irradiated volume. Thus, this study indicates that radiosurgery alone could be the method of choice for the treatment of a combination of AVM and aneurysm, if the aneurysm is close to or within the nidus.

72.

Year: 1998

Patient number: 76

Author: Aoki, S.; Sasaki, Y.; Machida, T.; Hayashi, N.; Shirouzu, I.; Ohkubo, T.; Terahara, A.; Sasaki, Y.; Kawamoto, S.; Araki, T.; Maehara, T.

Reference: Radiation medicine, 16, 4, 263-71, 1998

Title: 3D-CT angiography of cerebral arteriovenous malformations

Abstract: We studied 76 patients with cerebral arteriovenous malformations (AVMs) using dynamic-CT with intravenous injection of contrast material and reconstructed three-dimensional images (3D-CT angiography). All patients received stereotactic radiotherapy (gamma-knife). We compared 3D-CT angiography with conventional angiography to determine the usefulness of this technique. 3D-CT angiography could be performed in conjunction with usual axial high-resolution CT without any additional scanning time and within 10-30 minutes for the overall study. Most niduses and drainers of AVMs were clearly visualized by 3D-CT angiography. 3D-reconstruction was very helpful in demonstrating the niduses, drainers, and three-dimensional structure of AVMs. Demonstrations of feeders were not remarkable. Dynamic CT was very helpful in dose planning for gamma-knife radiosurgery, because gamma-knife angiograms were limited

in terms of angles, magnification, and establishing precise localizations using a head frame. 3D-CT added information on trails of drainers and was useful in reducing the volume of irradiation. 3D-CT angiography of cerebral AVMs could be performed routinely, and three-dimensional imaging was helpful in demonstrating the complex anatomy of cerebral AVMs. This technique was very helpful in planning gamma-knife radiosurgery.

73.

Year: 1998

Patient number: 332

Author: Flickinger, J. C.; Kondziolka, D.; Maitz, A. H.; Lunsford, L. D.

Reference: International journal of radiation oncology biology physics, 40, 2, 273-8, 1998

Title: Analysis of neurological sequelae from radiosurgery of arteriovenous malformations: how location affects outcome

Abstract: **PURPOSE/OBJECTIVE:** To elucidate how the risks of developing temporary and permanent neurological sequelae from radiosurgery for arteriovenous malformations (AVM) are related to AVM location, the addition of stereotactic magnetic resonance (MR) imaging to angiographic targeting, and prior hemorrhage or neurological deficits.

MATERIALS AND METHODS: We evaluated follow-up imaging and clinical data in 332 AVM patients who received gamma knife radiosurgery at the University of Pittsburgh between 1987 and 1994. All patients had regular clinical or imaging follow-up for a minimum of 2 years (range: 24-96 months, median = 45 months). There were 83 patients with MR- assisted planning, 187 with prior hemorrhages, and 143 with prior neurological deficits. **RESULTS:** Symptomatic postradiosurgery sequelae (any neurological problem including headache) developed in 30 (9%) of 332 patients. Symptoms resolved in 58% of patients within 27 months with a significantly greater proportion ($p = 0.006$) resolving in patients with $D_{min} < 20$ Gy vs. ≥ 20 Gy (89 vs. 36%). The 7-year actuarial rate for developing persistent symptomatic sequelae was 3.8%. We first evaluated the relative risks for different locations to construct a postradiosurgery injury expression (PIE) score for AVM location. Multivariate logistic regression analysis of symptomatic postradiosurgery sequelae identified independent significant correlations with PIE location score ($p = 0.0007$) and 12 Gy volume ($p = 0.008$), but with none of the other factors tested ($p > 0.3$), including the addition of MR targeting, average radiation dose in 20 cc, prior hemorrhage, or neurological deficit. We used these results to construct a risk prediction model for symptomatic postradiosurgery sequelae. The risk of radiation necrosis was significantly correlated with PIE score ($p < 0.048$), but not with 12-Gy volume. **CONCLUSION:** The risks of developing complications from AVM radiosurgery can be predicted according to location with the PIE score, in conjunction with the 12-Gy treatment volume. Further study of factors affecting persistence of these sequelae (progression to radiation necrosis) is needed.

74.

Year: 1998

Patient number: 82

Author: Heffez, D. S.; Osterdock, R. J.; Alderete, L.; Grutsch, J.

Reference: Surgical neurology, 49, 4, 373-81, 1998

Title: The effect of incomplete patient follow-up on the reported results of AVM radiosurgery

Abstract:BACKGROUND: The reported efficacy of AVM radiosurgery--80-85% 2-year obliteration rate--is based exclusively on the results of follow-up arteriography in a small percentage of treated patients; it is therefore inaccurate. We examined the effect of incomplete follow-up on the results of AVM radiosurgery. METHODS: We reviewed the results of AVM radiosurgery in 82 patients after a minimum of 24 months of follow-up. Patients were not preselected to undergo arteriography on the basis of any other imaging study. Data were analyzed using the Kaplan-Meier method and stratified by size of AVM. Results were compared with those obtained from the same data using the reporting techniques described in the literature. RESULTS: When data analysis was limited to patients who had follow-up arteriography, the 2-, 3-, and 4-year obliteration rates were 37%, 73%, and 84% after a minimum 24-month follow-up. Using Kaplan-Meier analysis the 2-, 3-, and 4-year obliteration rates were 32%, 55%, and 55% (95% CI = +/-18%), respectively. The 2-year obliteration rate was 43% for AVMs <30 mm in diameter and 16% for AVMs >30 mm in diameter, respectively. CONCLUSION: If data analysis is limited to the patients who undergo follow-up arteriography, the obliteration rate of AVM radiosurgery is overestimated. The actual 2-year obliteration rate if all data is considered is in the range of 40% rather than the commonly reported 80%. Therefore, treated patients are exposed to the risk of intracerebral hemorrhage for a longer period than previously appreciated. Compulsive long-term follow-up is required to document the true AVM obliteration rate after treatment by radiosurgery.

75.

Year: 1998

Patient number: 100

Author: Hodgson, T. J.; Zaman, S. M.; Cooper, J. R.; Forster, D. M.

Reference: British journal of neurosurgery, 12, 5, 434-7, 1998

Title: Proximal aneurysms in association with arteriovenous malformations: do they resolve following obliteration of the malformation with stereotactic radiosurgery?

Abstract:One-hundred consecutive patients were identified who had arteriovenous malformations (AVMs) treated by stereotactic radiosurgery (STRS) which were totally obliterated as shown by follow-up angiography. Of these cases, seven had intracerebral aneurysms at initial angiography, two of which were multiple. Five patients had saccular aneurysms at commonly recognized sites on the circle of Willis or main proximal cerebral arteries, while two patients had aneurysms on distal AVM feeder arteries in atypical sites (one saccular, one fusiform). Saccular aneurysms at typical sites were found to be unchanged in size following AVM obliteration. The significance of this finding in the management of patients who present with subarachnoid haemorrhage and who have both aneurysms and AVMs is discussed.

76.

Year: 1998

Patient number: 73

Author: Hou, Z.; Chen, Y.; Wu, X.

Reference: Chinese medical journal, 111, 11, 988-92, 1998

Title: The evaluation of MR localization for intracranial arteriovenous malformation treated with gamma knife

Abstract:OBJECTIVE: To evaluate the image quality, treatment effectiveness and complications of intracranial arteriovenous malformation (AVM) treated with gamma knife by MR localization. METHODS: According to Spetzler- Martin grading system, 73 intracranial AVMs were classified and treated with gamma knife by MR localization. The follow-up period was 6 to 34 months. The quality of MR localization image, the changes of AVM nidi after treatment were analyzed. Using ANOV (analysis of variance) statistic methods, we explored the relationship among the edema surrounding the AVM nidus, the radiation dosage and the AVM volume after treatment. RESULTS: The margin of AVM nidus was clear in all images. In the 73 images, MR signal of the local cranial skin and bone on the fixed points of head frame disappeared in 11 (15%), high or low shallow curve signals in the cerebral border occurred in 5 (7%) , the remaining 57 (78%) images had no artifacts. Based on the Spetzler-Martin grading score of AVM, the obliteration rates of AVM nidus were 100% in II, 88% in III, 57% in IV, 75% in V, 60% in VI during the 6-34 months follow-up after treatment. Edema around the AVM nidi occurred in 42 (57.5%) cases; among them, 27 were in slight degree, 10 in medium degree, and 5 in severe degree. Through ANOV statistic methods, we suggested that the degree of edema had no relation with the radiation dosage and AVM volume. Only one case had rebleeding 13 months after radiosurgery. CONCLUSION: MR localization for AVM treated with gamma knife is reliable and effective.

77.

Year: 1998

Patient number: 112

Author: Karlsson, B.; Kihlström, L.; Lindquist, C.; Steiner, L.

Reference: Neurosurgery, 42, 1, 1-5, 1998

Title: Gamma knife surgery for previously irradiated arteriovenous malformations

Abstract:OBJECTIVE: The goal was to report the treatment results after a second gamma knife treatment and to compare them with the results obtained after a first gamma knife treatment, as well as to investigate whether the models to predict the results after a first treatment are also applicable after gamma knife treatment of previously irradiated arteriovenous malformations. METHODS: The number of complications and the posttreatment hemorrhage rate were recorded for 112 patients in the study, and the number of obliterations was recorded for the 101 patients for whom conclusive angiograms were obtained. The results were compared with the expected results after a first gamma knife treatment. RESULTS: The observed number of obliterations was 62,

which is not significantly different from the predicted number of 65. There were 14 observed and 5 predicted complications. When the risk from the preceding radiation treatment was added, the observed number of complications was similar to the predicted number. Six hemorrhages were observed after the second treatment. Of the 5 patients with unchanged arteriovenous malformation size after both the first and second treatments, 2 experienced hemorrhages after the second treatment, compared with none among the 81 patients for whom the malformation was obliterated or significantly decreased in size after the second treatment. **CONCLUSIONS:** The obliteration rate after gamma knife surgery for previously irradiated arteriovenous malformations is similar to that after primary gamma knife treatment. The complication rate increases with the amount of radiation previously given. The incidence of posttreatment hemorrhages is lower in the latency period if the malformation is affected by the radiation.

78.

Year: 1998

Patient number: 127

Author: Kurita, H.; Kawamoto, S.; Sasaki, T.; Tago, M.; Kirino, T.

Reference: Japanese Journal of Neurosurgery, 7, 2, 95-101, 1998

Title: Indications and clinical results of gamma knife radiosurgery for a cerebral arteriovenous malformation

Abstract: Between June 1990 and August 1996, 351 patients with cerebral arteriovenous malformations (AVMs) underwent gamma knife radiosurgery in our institute. In 127 patients (36.2%), AVMs were located in central structure. The mean nidus volume treated was 2.7 ml, but ranged from 0.07 ml to 44.5 ml. The actuarial rate of angiographical obliteration of the nidus was 86.5% at 3 years. The obliteration rate did not depend on the nidus volume as long as a precise 3-D information was incorporated into the dose planning. The only factor significantly associated with the development of perinidal parenchymal change was AVM volume. In multivariate analysis, low flow of the malformation and a precise 3-D dose planning were the most significant factors associated with higher obliteration rate. Symptomatic radiation injury was observed in 7.4% of the patients. Permanent morbidity was 1.4%. Hemorrhage was suffered by 11 patients (3.1%) during the latency interval. The mortality due to bleeding was 45% and morbidity was 45%. The AVMs located in paraventricle areas were associated with higher risk of bleeding. Radiosurgery is a safe and valuable method to obliterate small deep seated AVMs. However, the limitations and adverse effects should be considered when planning radiosurgery for surgically accessible and/or large AVMs.

79.

Year: 1998

Patient number: 35

Author: Kurita, H.; Kawamoto, S.; Suzuki, I.; Sasaki, T.; Tago, M.; Terahara, A.; Kirino, T.

Reference: Journal of Neurology Neurosurgery and Psychiatry, 65, 5, 648-655, 1998

Title: Control of epilepsy associated with cerebral arteriovenous malformations after radiosurgery

Abstract:Objective. To investigate the effect of radiosurgery for symptomatic epilepsy associated with cerebral arteriovenous malformations (AVMs). Methods. Thirty five patients with unruptured epileptogenic AVMs were studied with a mean follow up of 43.0 months. The duration of epilepsy before radiosurgery ranged from 2 months to 21 years (mean 2.8 years). Fifteen patients showed partial seizures; eight of these had associated secondary generalisation. The remaining 20 patients showed only generalised seizures without preceding focal seizures. Results. At the final follow up examination, 28 patients remained seizure free, whereas seizures continued in seven. Variables significantly associated with continuity of seizures after radiosurgery were the number of seizures before therapy ($p < 0.01$) and duration of epilepsy ($p < 0.05$). According to Engel's classification, the 10 patients with intractable seizures before treatment included five with grade I, four with grade III, and one with grade IV. The frequency of seizures began to decrease several months after radiosurgery; much shorter than the time required for morphological change in the AVMs. Conclusions. Radiosurgery seems to be beneficial for seizure control in patients with unruptured epileptogenic AVM.

80.

Year: 1998

Patient number: 30

Author: Miyachi, S.; Tanaka, T.; Kobayashi, T.; Kida, Y.; Negoro, M.; Okamoto, T.; Yoshida, J.

Reference: Interventional Neuroradiology, 4, SUPPL. 1, 121-126, 1998

Title: Embolization of cerebral arteriovenous malformations to enhance the success of subsequent radiosurgery

Abstract:We studied angiographic changes in embolized arteriovenous malformations (AVMs) by comparing pre- and postembolization angiograms and angiograms preceding radiosurgery. This study sought factors determining the usefulness of embolization as a pretreatment to enhance the success of subsequent radiosurgery. Thirty patients with cerebral AVMs treated in this manner over 4 years were studied. In these cases AVMs were embolized with cyanoacrylate and were treated with Gamma-knife radiosurgery. The mean size of the AVM nidus was reduced by a fraction of seven following embolization. The subsequent angiogram for planning radiosurgery showed further nidus reduction in 10 AVMs, no change in 12, and regrowth in 8. In all size-reduction cases the nidus was sufficiently packed, and 2 AVMs had thrombosed completely before radiosurgery. All the regrowing AVMs were of diffuse type; 6 were associated with already-developed leptomeningeal channels, and the remaining 3 were fed by newly sprouted meningeal feeders. Five AVMs disappeared following radiosurgery, all representing size-reduction or no-change cases. Analysis of cases with regrowth showed increased risk of that event with feeder occlusion of a multi-axially supplied AVM, lack of reduction of shunt flow, or remaining meningeal feeders. On the other hand, when embolization as pretreatment prior to radiosurgery succeeds in producing a small, compacted, plexiform nidus with slow shunt flow, it furthers the likelihood of successful

radiosurgery. Nidus embolization and occlusion of fistulous and meningeal feeders are mandatory, while proximal feeder occlusion and use of embolic materials which risk recanalization should be avoided to prevent nidus regrowth.

81.

Year: 1998

Patient number: 30

Author: Mizoi, K.; Jokura, H.; Yoshimoto, T.; Takahashi, A.; Ezura, M.; Kinouchi, H.; Nagamine, Y.; Boku, N.

Reference: *Neurologia medico-chirurgica*, 38, 186-92, 1998

Title: Multimodality treatment for large and critically located arteriovenous malformations

Abstract: To define the current status of the multimodality treatment for large and critically located arteriovenous malformations (AVMs), we have made a retrospective review of 54 consecutive patients with Spetzler- Martin grade IV and V AVMs. The size of nidus is larger than 3 cm in diameter in all cases. Initially, all but one were treated by nidus embolization with the aim of size reduction. Only one patient had complete nidus occlusion by embolization alone. In 52 patients, the obliteration rate of nidus volume averaged 60% after embolization. Ten patients underwent complete surgical resection of AVMs following embolization with no postoperative neurological deterioration. Thirty-one patients underwent stereotactic radiosurgery following embolization. At the time of this analysis, 30 patients underwent follow-up angiography 2-3 years after radiosurgery. The results of radiosurgery correlated well with the preradiosurgical AVM volume. Of 16 patients with small residual AVMs (< 10 cm³, a mean volume of 4.7 cm³), nine (56%) had complete obliteration, and six (38%) had near- total or subtotal obliteration by 3 years after radiosurgery. In contrast, of 14 patients with large residual AVMs (> or = 10 cm³, a mean volume of 17.9 cm³), only two (14%) had complete obliteration, and eight (57%) had near-total or subtotal obliteration. Repeat radiosurgery was performed for the patients with remaining AVMs at 3- year follow-up review. This study indicates that a certain number of large and critically located AVMs can be safely treated by either microsurgery or radiosurgery following a significant volume reduction by nidus embolization. The present data also suggest the need and possible role of repeat radiosurgery in improving complete obliteration rate of large difficult AVMs, since many of those AVMs have significantly responded to initial radiosurgery.

82.

Year: 1998

Patient number: 220

Author: Pollock, B. E.; Flickinger, J. C.; Lunsford, L. D.; Maitz, A.; Kondziolka, D.

Reference: *Neurosurgery*, 42, 6, 1239-44, 1998

Title: Factors associated with successful arteriovenous malformation radiosurgery

Abstract: OBJECTIVE: To analyze the clinical and angiographic variables that affect the results of arteriovenous malformation (AVM) radiosurgery and to propose a new method

of reporting patient outcomes after AVM radiosurgery. This method incorporates both the obliteration status of the AVMs and the postoperative neurological condition of the patient. **METHODS:** Patient outcomes were defined as excellent (nidus obliteration and no new deficits), good (nidus obliteration with a new minor deficit), fair (nidus obliteration with a new major deficit), unchanged (incomplete nidus obliteration without a new deficit), poor (incomplete nidus obliteration with any new deficit), and dead. Two hundred twenty patients who underwent AVM radiosurgery at our center before 1992 were subjected to a multivariate analysis with patient outcomes as the dependent variable. **RESULTS:** Multivariate analysis determined four factors associated with successful AVM radiosurgery: smaller AVM volume ($P=0.003$), number of draining veins ($P=0.001$), younger patient age ($P=0.0003$), and hemispheric AVM location ($P=0.002$). Preradiosurgical embolization was a negative predictor of successful AVM radiosurgery ($P=0.02$). **CONCLUSION:** AVM obliteration without new neurological deficits can be achieved in at least 80% of patients with small volume, hemispheric AVMs after single-session AVM radiosurgery. Future studies on AVM radiosurgery should report patient outcomes in a fashion that incorporates all the factors involved in successful AVM radiosurgery.

83.

Year: 1998

Patient number: 66

Author: Sasaki, T.; Kurita, H.; Saito, I.; Kawamoto, S.; Nemoto, S.; Terahara, A.; Kirino, T.; Takakura, K.

Reference: Journal of neurosurgery, 88, 2, 285-92, 1998

Title: Arteriovenous malformations in the basal ganglia and thalamus: management and results in 101 cases

Abstract: OBJECT: Because arteriovenous malformations (AVMs) in the basal ganglia and thalamus are difficult to treat, the authors conducted a retrospective study to determine the best management strategy for these lesions. **METHODS:** The authors reviewed the management and outcome in 101 patients with AVMs treated between 1971 and 1995. In 15 conservatively treated patients, hemorrhage occurred in 71.4% (annual rate 11.4%), and the morbidity and mortality rates were 7.1% and 42.9%, respectively, during a mean follow-up period of 6.6 years. Total microsurgical resection was performed in 15 patients with no mortality resulting, but motor function deteriorated permanently in three of them (20%). Postoperative morbidity correlated well with the location of the AVM and with preoperative motor function. In cases of lenticular AVMs without motor weakness, a postoperative decrease in motor function was significantly more common than in the remaining patients. In patients with motor weakness before surgery, AVMs in the thalamus or caudate nucleus were successfully resected. Among 66 patients treated with gamma knife radiosurgery, three had permanent radiation-induced neurological deficits, and three others experienced bleeding (new bleeding in one case and rebleeding in two). The treatment-associated morbidity rate was 6.7%, and the actuarial rate of complete obliteration was 85.7% at 2.5 years. In five patients treated with embolization alone, the morbidity and mortality rates associated with the procedure or bleeding were

40% and 20%, respectively. The morbidity and mortality rates in the pre-gamma knife era were 22.2% and 22.2%, whereas those for the post-gamma knife era are currently 10.4% and 1.5%, respectively. **CONCLUSIONS:** These results indicate that conservatively treated AVMs are more likely to bleed and thus produce a high incidence of patient mortality. Multimodal treatment including radiosurgery, microsurgery, and embolization improved clinical outcomes by making it possible to treat difficult cases successfully.

84.

Year: 1998

Patient number: 53

Author: Yamamoto, M.; Hara, M.; Ide, M.; Ono, Y.; Jimbo, M.; Saito, I.

Reference: Surgical neurology, 49, 4, 385-97, 1998

Title: Radiation-related adverse effects observed on neuro-imaging several years after radiosurgery for cerebral arteriovenous malformations

Abstract:BACKGROUND: To our knowledge, there are no reported arteriovenous malformation (AVM) series in which detailed long-term follow-up results after radiosurgery were described based on the whole patient group. METHOD: We performed a detailed long-term follow-up study of 53 patients with cerebral AVMs treated with gamma knife (GK) radiosurgery, with emphasis on radiation-related adverse effects detected on neuro-imaging after a long post-irradiation latency period (3-10 years). The post-GK follow-up period was 40-232 months excluding two mortalities, the mean being 112 and the median being 111 months. RESULTS: Three patients (5.6%) have, as yet, refused all neuro-imaging follow-up studies. Complete nidus obliteration was confirmed angiographically in 32 patients (60.4%) between 1 and 5 post-GK years. In the other 18 patients (34%), despite significant nidus shrinkage being angiographically demonstrated, complete obliteration was not achieved during a 2-7 year follow-up period. There were two mortalities, one AVM-related (massive re-bleeding during the latency period) and the other angiography-related. There were five radiation-related morbidities (9.4%), three of which-hemi-Parkinson syndrome, hemiparesis, and visual field disturbances attributable to delayed cyst formation-manifested at 5.5, 7 and 7 post-GK years, respectively. We also experienced five patients (9.4%) in whom, despite remaining asymptomatic to date, radiation-related adverse effects were seen on neuro-imaging: middle cerebral artery stenosis at 3 post-GK years in one patient; dural arteriovenous fistula at 7 post GK-years in one; delayed cyst formation in two, at 5 and 10 post-GK years; and a small cavitation at 9 post-GK years. **CONCLUSION:** Long-term follow-up, particularly with neuro-imaging modalities, is essential even after the treatment goal has been attained.

85.

Year: 1997

Patient number: 307

Author: Flickinger, J. C.; Kondziolka, D.; Pollock, B. E.; Maitz, A. H.; Lunsford, L. D.

Reference: International journal of radiation oncology biology physics, 38, 3, 485-90, 1997

Title: Complications from arteriovenous malformation radiosurgery: multivariate analysis and risk modeling

Abstract: PURPOSE/OBJECTIVE: To assess the relationships of radiosurgery treatment parameters to the development of complications from radiosurgery for arteriovenous malformations (AVM). METHODS AND MATERIALS: We evaluated follow-up imaging and clinical data in 307 AVM patients who received gamma knife radiosurgery at the University of Pittsburgh between 1987 and 1993. All patients had regular clinical or imaging follow up for a minimum of 2 years (range: 24-96 months, median = 44 months). RESULTS: Post-radiosurgical imaging (PRI) changes developed in 30.5% of patients with regular follow-up magnetic resonance imaging, and were symptomatic in 10.7% of all patients at 7 years. PRI changes resolved within 3 years developed significantly less often ($p = 0.0274$) in patients with symptoms (52.8%) compared to asymptomatic patients (94.8%). The 7-year actuarial rate for developing persistent symptomatic PRI changes was 5.05%. Multivariate logistic regression modeling found that the 12 Gy volume was the only independent variable that correlated significantly with PRI changes ($p < 0.0001$) while symptomatic PRI changes were correlated with both 12 Gy volume ($p = 0.0013$) and AVM location ($p = 0.0066$). CONCLUSION: Complications from AVM radiosurgery can be predicted with a statistical model relating the risks of developing symptomatic post-radiosurgical imaging changes to 12 Gy treatment volume and location.

86.

Year: 1997

Patient number: 102

Author: Foroni, R.; Lonardi, S.; Nicolato, A.; Pasqualin, A.; Verlicchi, A.; Gerosa, M. A.; Bricolo, A.

Reference: Rivista Medica del Friuli, 3, 2, 89-95, 1997

Title: A feasible three-dimensional (3d) real time treatment planning system for gamma-knife radiosurgery of arterio-venous malformations (AVMs)

Abstract: Treatment optimization continues to represent a major issue in Gamma Knife Radiosurgery of endocranial arterio-venous malformations (AVMs) due to problems related to shape-recovery from bi-dimensional angiography, 3D volume reconstruction of the nidus, proper positioning of the shots, and accurate target/isodose matching. The author's recent clinical trial experience with phantoms indicate that heuristic procedures may provide suitable operative models. The aim of this study is to integrate the 3D volume of the target lesion with the 3D resulting isodose at a multifocal dose-planning. The sequence of the computerized flow diagram used is easily summarized: 1) Definition of the double outline contour (xz, yz plans) of the nidus silhouette. 2) 3D shape recovery and calculation of the target volume. 3) Projection of the AVM-nidus along the xy, xz, and yz axes. 4) Positioning on each of the three plans of one or more shots with coordinates relative to the matrix center calculated in real time. 5) Real time visualization of the graphic projection of the preferred isodose contour with final 'routine' calculation of the treatment program. 6) Evaluation and further validation of the radiosurgical program along the three different axes. Clinical experience in a preliminary series of 102

intracranial A VMs seems to confirm the importance and advantages of this approach. Specifically: Treatment programs may be calculated and performed based on three-dimensional logic. The real geometrical congruence between lesion shape and matching isodose can be properly assessed under mathematical conditions.

87.

Year: 1997

Patient number: 1128

Author: Karlsson, B.; Lax, I.; Söderman, M.

Reference: Radiotherapy and oncology, 43, 3, 275-80, 1997

Title: Factors influencing the risk for complications following Gamma Knife radiosurgery of cerebral arteriovenous malformations

Abstract:BACKGROUND AND PURPOSE: We reported previously a model predicting the risk for radiation-induced complications following Gamma Knife radiosurgery for AVM. No factor other than the dose distribution was related to the risk. The aim of this study was to define if other parameters are of importance for the risk of complications. MATERIAL AND METHODS: The model above was used to calculate the risk for complications in all 1128 AVM patients Gamma Knife-treated at the Karolinska Hospital 1970-1993. The number of predicted complications was compared to the number of observed ones for a number of different parameters. RESULTS: The model underestimated the risk of complications for patients previously given radiation with multiple or single fractions. Neither age nor gender influenced the risk of complications. Centrally located AVM had a higher, and peripheral a lower incidence of complications as compared to the calculated risk, and a previous hemorrhage reduced the risk of complications. From the observed number of complications, parameters in the model were determined by a fitting procedure separately for three groups of AVM: central and peripheral with and without a previous hemorrhage. It is also shown that the assumption of a serial functional architecture is valid in the model. This was investigated by the use of a relative seriality model with a combined serial-parallel functional architecture. CONCLUSIONS: The risk of complications following radiosurgical treatment of AVM is dependent on the clinical history, AVM location and whether the patient has received radiation earlier. Grant ID: P30 CA 21765, Acronym: CA, Agency: NCI.

88.

Year: 1997

Patient number: 945

Author: Karlsson, B.; Lindquist, C.; Steiner, L.

Reference: Neurosurgery, 40, 3, 425-30, 1997

Title: Prediction of obliteration after gamma knife surgery for cerebral arteriovenous malformations

Abstract:OBJECTIVE: To define the factors of importance for the obliteration of cerebral arteriovenous malformations (AVMs), thus making a prediction of the probability for

obliteration possible. **METHODS:** In 945 AVMs of a series of 1319 patients treated with the gamma knife during 1970 to 1990, the relationship between patient, AVMs, and treatment parameters on the one hand and the obliteration of the nidus on the other was analyzed. **RESULTS:** The obliteration rate increased both with increased minimum (lowest periphery) and average dose and decreased with increased AVM volume. The minimum dose to the AVMs was the decisive dose factor for the treatment result. The higher the minimum dose, the higher the chance for total obliteration. The curve illustrating this relation increased logarithmically to a value of 87%. A higher average dose shortened the latency to AVM obliteration. For the obliterated cases, the larger the malformation, the lower the minimum dose used. This prompted us to relate the obliteration rate to the product minimum dose (AVM volume)^{1/3} (K index). The obliteration rate increased linearly with the K index up to a value of approximately 27, and for higher K values, the obliteration rate had a constant value of approximately 80%. For the group of 273 cases treated with a minimum dose of at least 25 Gy, the obliteration rate at the study end point (defined as 2-yr latency) was 80% (95% confidence interval = 75-85%). If obliterations that occurred beyond the end point are included, the obliteration rate increased to 85% (81-89%). **CONCLUSION:** The probability of obliteration of AVMs after gamma knife surgery is related both to the lowest dose to the AVMs and the AVM volume, and it can be predicted using the K index.

89.

Year: 1997

Patient number: 18

Author: Kihlström, L.; Guo, W. Y.; Karlsson, B.; Lindquist, C.; Lindqvist, M.

Reference: Journal of neurosurgery, 86, 4, 589-93, 1997

Title: Magnetic resonance imaging of obliterated arteriovenous malformations up to 23 years after radiosurgery

Abstract: The authors report outcomes in 18 patients with arteriovenous malformations (AVMs) who were treated with gamma knife radiosurgery and in whom magnetic resonance (MR) imaging was obtained a mean of 14 years (range 8-23 years) after treatment and 10 years (range 4-17 years) after confirmed obliteration of the AVM. All patients were asymptomatic after radiosurgery and during the time of the study. In five patients (28%), cyst formation was observed that corresponded to the site of the obliterated AVM. Cyst formation and contrast enhancement on MR imaging could not be statistically correlated to the radiation dose. In 11 (61%) of the 18 patients, contrast enhancement that was not related to a recanalization of the nidus was observed in the target area. In three patients (17%), an increased T2-weighted signal was detected at the site of previous AVM; this was interpreted as gliosis or demyelination, which appeared to be dose dependent. The study illustrates that cyst formation, contrast enhancement, and an increased T2-weighted signal can be observed in asymptomatic patients in the area that was targeted for AVM radiosurgery up to 23 years after the procedure. The report provides new and essential information about long-term effects on normal tissue after radiosurgery and provides a basis for the interpretation of MR studies in the follow up of small AVMs treated by radiosurgery.

90.

Year: 1997

Patient number: 43

Author: Van, Rooij W. J. J.; Sluzewski, M.; Wijnalda, D.; Schellens, R. L. L. A.; Verhagen, I. T. H. J.; Karlsson, B.

Reference: Nederlands Tijdschrift voor Geneeskunde, 141, 44, 2111-2117, 1997

Title: Multidisciplinary treatment of cerebral arteriovenous malformations; preliminary results in 115 consecutive patients

Abstract:Objective. Preliminary evaluation of the combined treatment (surgery, embolization and stereotactic gamma radiosurgery) of 115 consecutive patients with a cerebral arteriovenous malformation (AVM). Design. Retrospective. Setting. St. Elisabeth Hospital, Tilburg, the Netherlands. Patients and methods. In a 35-month period 115 consecutive patients presented with an AVM. The mean age was 41.8 years (range: 6-72). The main clinical presentation was haemorrhage in 65 patients (56.5%), seizures in 31 patients (27.0%), neurological deficit in 7 patients (6.1%) and hydrocephalus in 2 patients (1.7%); in 10 patients (8.7%) the AVM was an incidental finding. Treatment consisted of surgery, radiosurgery with the gamma knife and embolization. Embolization was mostly used to reduce the size of an AVM before surgery or radiosurgery. Results. Out of 115 patients 5 were referred for a treatment advice only and treatment was performed elsewhere. Of the remaining 110 patients 84 (76.4%) were treated and 26 (23.6%) were not treated for various reasons. Of the 84 treated patients 17 (20.2%) had surgery only, 17 (20.2%) had radiosurgery only, and 12 (14.3%) were treated with embolization only. Surgery after embolization was performed in 8 patients (9.5%) and radiosurgery after embolization in 26 patients (31.0%). In 4 patients an unusual combination of these treatment methods was used for a variety of reasons. At the time of writing 35 of 84 treated AVMs (41.7%) were completely cured, 39 patients were awaiting the definitive result of radiosurgery. Deliberate partial embolization was performed in 5 patients. In 5 patients (6.0%), the pretreatment objective was not achieved with embolization. Total permanent morbidity was 4.8% (4 patients) and mortality was 1.2% (1 patient). Conclusion. Given a multidisciplinary combination of treatment methods a treatment is indicated and possible in the majority (76.4%) of patients with an AVM. There is a reasonable chance of a complete cure with an acceptable complication rate.

91.

Year: 1997

Patient number: 93

Author: Wowra, B.; Horstmann, G. A.; Cibis, R.; Czempiel, H.

Reference: Der Radiologe, 37, 12, 1003-15, 1997

Title: Profile of ambulatory radiosurgery with the gamma knife system 2: Report of clinical experiences

Abstract:Gamma Knife radiosurgery (GKRS) was applied in 500 consecutive treatments

for 445 patients within 2 years. Indications were arterio-venous malformations (93 patients), schwannomas of cranial nerves (75 patients), meningiomas (79 patients; 73 of the tumors involving the skull base), pituitary adenomas (40 patients), craniopharyngiomas (13 cases), gliomas (13 cases), rare indications (12 cases), and brain metastases (126 patients). In arterio-venous malformations two complications were observed whereas two other patients underwent surgery due to intracranial hemorrhage in the latent period after GKRS. In all cases follow-up with MRI showed evidence of an active obliteration process. Out of 24 patients with a follow-up over 1 year, angiography revealed complete obliteration in 9 patients so far. A partial obliteration was evidenced by MRI in 15 cases. In benign tumors (meningiomas and vestibular schwannomas) tumor control rates of 88% and 89% were achieved, respectively. Treatment related side effects were mild and rare; no facial palsy occurred after primary Gamma Knife treatment. GKRS was particularly effective in inoperable skull base meningiomas. Cerebral metastases were controlled in 89.5% by a single Gamma Knife treatment. The mean survival period was 11.8 months. In patients receiving a single Gamma Knife treatment the mean survival time was 9.1 months. For patients undergoing multiple (up to 5) sessions of GKRS (because of new tumors) the mean survival period was 17.2 months. MRI showed evidence of adverse radiation reactions in 10/124 patients (8.1%) which were symptomatic in 3 patients (0.8%). The results obtained in patients with cerebral metastases emphasize that GKRS alone is as effective as the combined treatment of these lesions by surgery and fractionated radiotherapy. Our results demonstrated an attractively high therapeutic gain factor of Gamma Knife treatment in key indications of radiosurgery.

92.

Year: 1996

Patient number: 27

Author: Aigner, R. M.; Leber, K.; Nicoletti, R.; Fueger, G. F.

Reference: Nuclear medicine communications, 17, 10, 877-83, 1996

Title: Semi-quantitative scintigraphic follow-up studies of cerebral arteriovenous malformations after radiosurgical treatment

Abstract: An evaluation of semi-quantitative ⁹⁹Tc^m-red blood cell scintigraphy (RBCS) was undertaken in patients with cerebral arteriovenous malformations (AVM) during follow-up after radiosurgical treatment. Twenty-seven patients were studied with an initial dynamic imaging sequence of 32 frames each lasting 2 s, planar images in four projections beginning 15 min post-injection and single photon emission tomography immediately following the planar imaging. A 2 ml cubital vein blood sample was imaged to obtain an extracorporeal equivalent of the intravascular activity. The counts within the AVM on a planar image were divided by the counts obtained from the image of the blood sample (corrected for the same acquisition time and radioactive decay). This value yielded the 'volume index' (VI), which was proportional to the volume of the AVM. The VI obtained from the first RBCS served as the initial reference value and was set at 100%. The VIs obtained from the follow-up investigations of the same patient in the same projection were expressed as the percentage of the initial VI. We found RBCS identified

the AVM in all patients. The VIs obtained from the follow-up studies demonstrated a decrease in blood volume at different time intervals after radiosurgical treatment. RBCS provides a sensitive, relatively non-invasive, semi-quantitative method for measuring the relative volume and follow-up of the degree of obliteration of AVMs after radiosurgical treatment.

93.

Year: 1996

Patient number: 236

Author: Aoki, Y.; Nakagawa, K.; Tago, M.; Terahara, A.; Kurita, H.; Sasaki, Y.

Reference: Radiation medicine, 14, 5, 265-8, 1996

Title: Clinical evaluation of gamma knife radiosurgery for intracranial arteriovenous malformation

Abstract: **PURPOSE:** Aim of the study is to compare our treatment results of gamma knife radiosurgery for arteriovenous malformation (AVM) and to obtain factors determining nidus obliteration and/or adverse effect. **METHODS:** We analyzed 236 patients with AVM treated between June 1990 and February 1994. The patients consisted of 137 men and 99 women, and ranged in age from 4 to 71 years. AVM volume ranged 0.7 to 37.7 ml. Maximum and peripheral doses ranged from 18.2 to 60.0 Gy and 10.0 to 28.0 Gy, respectively. **RESULTS:** Complete obliteration rates at 1, 2, and 3 years were 36.2, 68.9, and 86.6%, respectively. The mean time to complete obliteration was 21.4 months. Univariate analysis revealed that calculated target volume, peripheral dose, peripheral percent dose and treatment optimality were significant factors for complete obliteration. In multivariate analysis, calculated target volume, treatment optimality, and CT-based planning were significant factors. The actuarial risk of post-radiosurgical brain edema at 2 years was 20.0%. In both univariate and multivariate analysis, calculated target volume was the only significant factor. Symptomatic complications developed in 10.0% of patients at 2 years, but no significant factors were identified. Permanent complications and severe neurological deficits were seen in 4.4 and 2.8% of patients, respectively. **CONCLUSIONS:** Our results were similar to those reported previously. Accurate CT-based planning contributed to an improved obliteration rate.

94.

Year: 1996

Patient number: 27

Author: Baumann, G. S.; Wara, W. M.; Larson, D. A.; Sneed, P. K.; Gutin, P. H.; Ciricillo, S. F.; McDermott, M. W.; Park, E.; Stalpers, L. J.; Verhey, L. J.; Smith, V.; Petti, P. L.; Edwards, M. S.

Reference: Pediatric neurosurgery, 24, 4, 193-201, 1996

Title: Gamma knife radiosurgery in children

Abstract: 52 pediatric patients were treated with radiosurgery at the University of California, San Francisco. Arteriovenous malformations were treated in 27 patients.

Complete obliteration was noted in 4 of 12 patients imaged more than 2 years after radiosurgery. Arteriovenous malformation rebleed was noted in 1 patient. Symptomatic T2 changes were noted in 2 patients. Among 29 neoplasms treated in 25 patients, local control was noted in 5 of 7 low-grade gliomas, 5 of 14 high-grade gliomas, 4 of 5 craniopharyngiomas and 3 of 3 sarcomas. Three patients treated for neoplasms developed necrosis after radiosurgery.

95.

Year: 1996

Patient number: 197

Author: Flickinger, J. C.; Pollock, B. E.; Kondziolka, D.; Lunsford, L. D.

Reference: International journal of radiation oncology biology physics, 36, 4, 873-9, 1996

Title: A dose-response analysis of arteriovenous malformation obliteration after radiosurgery

Abstract: **PURPOSE:** Although radiosurgery is effective in obliterating the pathologic vessels of intracranial arteriovenous malformations (AVM), the relationships of both dose and volume to obliteration have not been well defined. **METHODS AND MATERIALS:** The results of radiosurgery in 197 AVM patients with 3-year angiographic follow-up were analyzed. Volume varied from 0.06-18 cc (median: 4.1 cc), and minimum target dose (Dmin) varied from 12.0-25.6 Gy (median: 20.0 Gy). **RESULTS:** Follow-up angiography revealed complete AVM obliteration in 142 out of 197 patients (72%). The targeted AVM nidus failed to obliterate in 20 patients (10%), but in-field obliteration was complete in the remaining 35 patients (18%) discovered to have residual untargeted AVM nidus. Multivariate logistic regression analysis of in-field obliteration revealed a significant independent correlation with Dmin ($p = 0.04$), but not with volume or maximum dose. A sigmoid dose-response curve for in-field obliteration was constructed that significantly differed from the dose-volume-response relationships that would have been expected from overall obliteration data. **CONCLUSIONS:** The success rate for in-field obliteration of AVM after radiosurgery depends on Dmin but does not appear to change appreciably with volume or maximum dose. Success rates for complete obliteration additionally are limited by problems defining the complete AVM nidus.

96.

Year: 1996

Patient number: 72

Author: Gerszten, P. C.; Adelson, P. D.; Kondziolka, D.; Flickinger, J. C.; Lunsford, L. D.

Reference: Pediatric neurosurgery, 24, 3, 139-44, 1996

Title: Seizure outcome in children treated for arteriovenous malformations using gamma knife radiosurgery

Abstract: Seizures are the second most common presenting symptom of arteriovenous malformations (AVMs) in children. Although radiosurgery has been found to be a safe and effective alternative treatment, the outcome of seizure control in children after

radiosurgery for AVMs is unknown. Between 1987 and 1994, 72 children under the age of 18 years were treated with gamma knife radiosurgery for AVMs at our institution. Fifteen patients (21%) had seizures as part of their clinical course. There were 11 boys and 4 girls with ages varying from 2 to 17 years (median 16 years). Seizures included: generalized tonic-clonic (n = 8); focal motor or sensory (n = 4); partial complex (n = 2), and a combination of generalized and partial complex (n = 1). Nine lesions were in cortical locations; six were subcortical. Spetzler-Martin grades included: II (n = 7); III (n = 4); IV (n = 2), and VI (n = 2). During follow-up after radiosurgical treatment, 11 of 13 patients (85%) were seizure free and off anticonvulsant therapy (mean follow-up 47 months). Two patients had a significant improvement in their seizures but continue on medication. Two of the 72 patients (3%) developed seizures after treatment and remain on medication. Seizure outcome was not associated with the location or complete obliteration of the lesion. We conclude that stereotactic radiosurgery, as a non-invasive alternative, is associated with a good outcome for the AVM as well as AVM-related seizures in children.

97.

Year: 1996

Patient number: 16

Author: Guo, W. Y.; Pan, H. C.; Chung, W. Y.; Wang, L. W.; Teng, M. M.

Reference: Stereotactic and functional neurosurgery, 66, Suppl 1, 71-84, 1996

Title: Do we need conventional angiography? The role of magnetic resonance imaging in verifying obliteration of arteriovenous malformations after Gamma Knife surgery

Abstract: Sixteen cerebral arteriovenous malformations (AVMs) were examined to determine the role of magnetic resonance (MR) imaging in verifying obliteration. The AVMs (mean volume 7.5 cm³, range 2-17 cm³) were treated with Gamma Knife surgery between March 1993 and May 1994. Integration of stereotactic MR and stereotactic conventional X-ray angiography (XRA) was used for targeting in the Gamma Knife surgery. All MR examinations both for targeting and follow-up, were performed on a 1.5-Tesla superconductive MR scanner (Signa). Multiple pulse sequences (spin echo T1- and T2-weighted MR imaging, and three-dimensional time-of-flight MR angiography) were used. The mean maximum target dose was 37.4 Gy (range 25.0-44.0 Gy). The mean minimum target dose was 20.1 Gy (range 17.5-25.2 Gy). Follow-up imaging was performed about every 6 months or when clinically warranted. XRA was performed when the AVM was no longer seen on MR images. The time from the last

98.

Year: 1996

Patient number: 1604

Author: Karlsson, B.; Lindquist, C.; Steiner, L.

Reference: Minimally invasive neurosurgery, 39, 1, 21-7, 1996

Title: Effect of Gamma Knife surgery on the risk of rupture prior to AVM obliteration

Abstract: The incidence for hemorrhage in non-obliterated arteriovenous malformations

(AVM) during the first two years following Gamma Knife (GK) surgery was compared to the calculated incidence in untreated patients. There was a decrease in the incidence of hemorrhage as compared to the natural course. This difference was statistically significant. The actual number of hemorrhages during the first two years was 49 in a series of 1604 patients. Additionally, 41 hemorrhages occurred beyond the two years following treatment over the entire follow up time span of up to 24 years. For the first two years the calculated incidence was roughly two times higher than the observed incidence. This impact on the natural history was detectable already within six months after the treatment for the malformations totally covered with at least 25 Gy. The relation between a high minimum and a high average dose on the one hand and a lower risk for hemorrhage on the other hand was statistically significant. Low treatment doses and high age correlated to a higher risk. Neither hemorrhage prior to treatment nor time interval between presenting hemorrhage and treatment seemed to influence the risk for post treatment hemorrhage. The risk for permanent neurological deficit or death due to AVM rupture during the latency period between the time of treatment and total nidus obliteration was less than 0.5% for small AVM and 2-4% for large ones during the first two years. Of the 24 patients with sequelae following AVM rupture after treatment 14 died and 10 remained with neurological deficit of different degrees. However, all survivors were self sufficient.

99.

Year: 1996

Patient number: 71

Author: Kobayashi, T.; Tanaka, T.; Kida, Y.; Oyama, H.; Niwa, M.; Maesawa, S.

Reference: No to shinkei, 48, 4, 351-6, 1996

Title: Gamma knife treatment of AVM of the basal ganglia and thalamus

Abstract: Arteriovenous malformations (AVMs) in the basal ganglia (BG) and thalamus (Thal) are difficult to treat by microsurgery or intravascular embolization alone, and the role of stereotactic gamma radiosurgery (gamma knife) of these AVMs is discussed. We have treated 324 cases of AVM with gamma knife since May 1991, and in 71 of these cases (19%) the AVM was in the BG or Thal. The results of gamma radiosurgery on AVMs of the BG and Thal were compared with the results of treating AVMs at other intracranial locations by gamma radiosurgery. The nidi were small (mean diameter: 16.4 mm), and they were treated with a mean maximum dose of 36.4 Gy and marginal dose of 19.9 Gy. The results were evaluated angiographically in 39 (55%) of the 71 cases, with a mean follow-up period of 23 months. The complete obliteration rate of AVMs in the BG and Thal 1 and 2 years after treatment was 54.3% and 92.0%, respectively, and the rate at the other locations was 42.9% and 76.0%, respectively. Adverse effects of this treatment in the AVM cases overall were rebleeding from the nidus in 5 cases (1.5%) and radiation necrosis in 4 cases (1.2%). In conclusion, AVMs of the BG and Thal were effectively and safely treated with the gamma knife, and stereotactic radiosurgery is a definitive alternative treatment for deep seated AVMs.

100.

Year: 1996

Patient number: 21

Author: Morikawa, M.; Numaguchi, Y.; Rigamonti, D.; Kuroiwa, T.; Rothman, M. I.; Zoarski, G. H.; Simard, J. M.; Eisenberg, H.; Amin, P. P.

Reference: International journal of radiation oncology biology physics, 34, 3, 663-75, 1996

Title: Radiosurgery for cerebral arteriovenous malformations: assessment of early phase magnetic resonance imaging and significance of gadolinium- DTPA enhancement

Abstract:**PURPOSE:** To evaluate the initial changes within the nidus of arteriovenous malformations (AVMs) and to assess the reaction to the brain tissue surrounding AVMs after radiosurgery by serial magnetic resonance (MR) imaging. **METHODS AND MATERIALS:** Twenty-one patients, treated using ⁶⁰Co gamma knife unit with cerebral AVMs, were retrospectively evaluated. Forty-seven follow-up MR images of the 21 patients were performed including 10 patients with two or more serial gadolinium enhanced studies (Gd-MR). Two or more sequential MR angiographies (MRA) were obtained in 13 patients. Three-dimensional (3D) time-of-flight MRA and two-dimensional (2D) phase contrast MRA were used in 13 patients for evaluating the flow changes of AVMs. The follow-up period after radiosurgery ranged from 3 to 30 months (average 10.8 months) and the interval time of MRI ranged from 34 days to 13 months (average 4.9 months). **RESULTS:** Reduction of nidus size was observed in 14 of 21 patients (67%) between 4 to 13 months on spin echo (SE) images. Complete obliteration was observed on SE images in 4 of these 14 patients; three were confirmed by conventional angiography. New hyperintense areas surrounding the nidus on T2s- weighted images (T2WI) developed in 9 of the 14 patients who showed nidus reduction between 5 to 17 months after radiosurgery; in three patients, size of the hyperintense area started to decrease between 6 to 7 months after its appearance. Probable radiation necrosis of pons developed in one patient 26 months after radiosurgery. The irradiated area within the AVM nidus was significantly enhanced in 8 of the 10 patients who underwent Gd-MR. The degrees of enhancement within the nidus increased with time in 7 of the 10 patients. Overall, total enhancement of irradiated areas was observed in four of the 10 patients; in three of the four, the enhancement decreased in size and degree, indicating nidus reduction. In three patients who had a partial volume irradiation within the nidus, the enhancing areas corresponded with the exact portions of irradiated volume. The nidus reduction was observed in 7 of the 13 patients on MRA during 5 to 13 months after radiosurgery. MRA was more useful compared to SE images in four of the seven patients in evaluating the size change of AVM nidus, feeding arteries, and draining veins. **CONCLUSION:** Magnetic resonance imaging and MRA were useful in assessing the progress of nidus reduction. T2-weighted imaging was sensitive to radiation- induced reaction in and around the AVM nidus. The enhancement within the AVM nidus on Gd-MR may represent the initial sign of nidus reduction and demonstrates the exact location of irradiation in the nidus. The changes of the enhancement pattern are presumed to represent the processes of nidus reduction and irradiated reaction within the AVM nidus.

101.

Year: 1996

Patient number: 315

Author: Pollock, B. E.; Flickinger, J. C.; Lunsford, L. D.; Bissonette, D. J.; Kondziolka, D.

Reference: Neurosurgery, 38, 4, 652-9, 1996

Title: Hemorrhage risk after stereotactic radiosurgery of cerebral arteriovenous malformations

Abstract: To analyze the effect of stereotactic radiosurgery on the hemorrhage rate of arteriovenous malformations (AVMs), we reviewed the clinical and angiographic characteristics of 315 patients with AVMs before and after radiosurgery. One hundred ninety-six patients sustained 263 bleeds in 10,939 patient-years before radiosurgery, for an annual nonfatal hemorrhage rate of 2.4%. Clinical follow-up after radiosurgery was available in 312 patients (mean, 47 +/- 20 mo); follow-up > or = 24 months was obtained in 295 patients (94%). Twenty-one patients had AVM bleeds at a median of 8 months (range, 1-60 mo) after radiosurgery. Two additional patients had three aneurysmal bleeds (at 5, 27, and 32 mo, respectively) for a 7.4% total risk of hemorrhage per patient. The actuarial hemorrhage rate until AVM obliteration was 4.8% per year (95% confidence interval, 2.4-7.0%) during the first 2 years after radiosurgery and 5.0% per year (95% confidence interval, 2.3-7.3%) for the third to fifth years after radiosurgery. Multivariate analysis of clinical and angiographic factors demonstrated that the presence of an unsecured proximal aneurysm was associated with an increased risk of postradiosurgical hemorrhage (relative risk, 4.56; 95% confidence interval, 1.77-11.70%; P < 0.001). No AVM hemorrhages were observed after radiosurgery in seven patients with intranidal aneurysms. No protective effect against hemorrhage was observed in patients who received an optimal radiation dose (> or = 25 Gy to the AVM margin) compared with patients who received < 25 Gy to the AVM margin (P = 0.36). No patient suffered a hemorrhage after angiography had confirmed complete obliteration (n = 140) or suffered from an early draining vein without residual nidus (n = 19). Stereotactic radiosurgery was not associated with a significant change in the hemorrhage rate of AVMs during the latency interval before obliteration. No protective benefit was conferred on patients who had incomplete nidus obliteration in early (< 60 mo) follow-up after radiosurgery. AVM patients with unsecured proximal aneurysms should have aneurysms obliterated either before radiosurgery or at the time of surgical resection of their AVMs.

102.

Year: 1996

Patient number: 315

Author: Pollock, B. E.; Flickinger, J. C.; Lunsford, L. D.; Bissonette, D. J.; Kondziolka, D.

Reference: Stroke, 27, 1, 1-6, 1996

Title: Factors that predict the bleeding risk of cerebral arteriovenous malformations

Abstract: BACKGROUND AND PURPOSE: Arteriovenous malformations (AVMs) have an overall 2% to 4% annual risk of hemorrhage. The purpose of this study was to

determine whether specific clinical and radiographic factors predispose AVMs to bleed and to predict the bleeding risk for individual AVM patients. **METHODS:** We reviewed the clinical histories and cerebral angiograms of 315 AVM patients who underwent stereotactic radiosurgery at our center. One half of the patient data (analysis cohort) was used to determine risk factors for bleeding and to construct AVM hemorrhage risk groups. These risk groups were then tested with the second half of the patient data (test cohort). **RESULTS:** The mean AVM volume was 4.0 +/- 3.4 mL (approximate maximum diameter of 2 cm). One hundred ninety-six initial hemorrhages occurred in 10,348 patient-years for an annual initial bleed rate of 1.89%; 44 of these 196 patients had a repeat bleed in 591 patient-years for an annual rebleed rate of 7.45%. The overall crude annual hemorrhage rate was 2.40%. Multivariate analysis revealed three factors associated with hemorrhage: history of a prior bleed (relative risk (RR), 9.09; 95% confidence interval (CI), 5.44 to 15.19; P < .001), a single draining vein (RR, 1.66; 95% CI, 1.13 to 2.38; P < .01), and a diffuse AVM morphology (RR, 1.64; 95% CI, 1.12 to 2.46; P < .01). Four AVM hemorrhage risk groups were constructed on the basis of the significant factors. The annual rate of bleeding was 0.99% for low- risk AVMs, 2.22% for intermediate-low-risk AVMs, 3.72% for intermediate-high-risk AVMs, and 8.94% for high-risk AVMs. **CONCLUSIONS:** Analysis of a large group of AVM patients who underwent stereotactic radiosurgery demonstrated that small AVMs have an annual hemorrhage risk similar to that of the general AVM population. AVM patients have a wide variability of bleeding risk that can be predicted from their clinical presentation and the angiographic characteristics of the AVM. The management of AVM patients should be based not only on the morbidity of the proposed treatment but also those factors that predispose individual patients to either a low or high hemorrhage risk.

103.

Year: 1996

Patient number: 140

Author: Pollock, B. E.; Kondziolka, D.; Flickinger, J. C.; Patel, A. K.; Bissonette, D. J.; Lunsford, L. D.

Reference: Journal of neurosurgery, 85, 6, 1044-9, 1996

Title: Magnetic resonance imaging: an accurate method to evaluate arteriovenous malformations after stereotactic radiosurgery

Abstract: To determine the accuracy of magnetic resonance (MR) imaging in comparison to cerebral angiography after radiosurgery for an arteriovenous malformation (AVM), the authors reviewed the records of patients who underwent radiosurgery at the University of Pittsburgh Medical Center before 1992. All patients in the analysis had AVMs in which the flow-void signal was visible on preradiosurgical MR imaging. One hundred sixty-four postradiosurgical angiograms were obtained in 140 patients at a median of 2 months after postradiosurgical MR imaging (median 24 months after radiosurgery). Magnetic resonance imaging correctly predicted patency in 64 of 80 patients in whom patent AVMs were seen on follow-up angiography (sensitivity 80%) and angiographic obliteration in 84 of 84 patients (specificity 100%). Overall, 84 of 100 AVMs in which evidence of obliteration was seen on

104.

Year: 1996

Patient number: 45

Author: Pollock, B. E.; Kondziolka, D.; Lunsford, L. D.; Bissonette, D.; Flickinger, J. C.

Reference: Neurosurgery, 38, 2, 318-24, 1996

Title: Repeat stereotactic radiosurgery of arteriovenous malformations: factors associated with incomplete obliteration

Abstract: Second stereotactic radiosurgery procedures were required in 45 patients with arteriovenous malformations (AVMs) who initially had incomplete obliteration. Repeat radiosurgery was performed at a median of 39 months (range, 24-71 mo) after the first stage. The median AVM volume at the first procedure was 6.0 ml (range, 0.2-18.0 ml). Thirty-seven patients (82%) had AVMs of Spetzler-Martin Grades III through VI. A retrospective analysis revealed definite causes for incomplete obliteration after the first procedure in 33 patients (73%). Incomplete angiographic definition of the nidus was the most frequent factor (57%) associated with failed radiosurgery. Three patients (7%) had recanalization of the AVM nidus after prior embolization; four patients (9%) had incomplete nidus recognition, because AVM vessels were not visualized in the presence of a hematoma. Radiobiological resistance was another potential factor associated with failed radiosurgery in 17 patients (38%). Our current technique for volume determination and dose planning includes stereotactic magnetic resonance angiography, magnetic resonance imaging, and complete cerebral angiography (including superselective and external carotid artery injections, as indicated). Integrated multiplanar high-resolution imaging will likely increase the rate of AVM obliteration after stereotactic radiosurgery.

105.

Year: 1996

Patient number: 34

Author: Pollock, B. E.; Lunsford, L. D.; Kondziolka, D.; Bissonette, D. J.; Flickinger, J. C.

Reference: Journal of neurosurgery, 84, 3, 437-41, 1996

Title: Stereotactic radiosurgery for postgeniculate visual pathway arteriovenous malformations

Abstract: Arteriovenous malformations (AVMs) that are located within the postgeniculate optic radiations or striate cortex are difficult to resect without creating postoperative visual defects. To reduce the risk of an AVM hemorrhage and to enhance the possibility of preserving visual function, the authors performed stereotactic radiosurgery in 34 patients with newly diagnosed or residual AVMs of the visual pathways. The mean AVM volume was 4.7 ml, and the average radiation dose to the AVM margin was 21 Gy. The median follow up was 47 months (range 16-83 months). Two (6%) of 34 patients had documented new visual field defects (central scotoma in one, and partial hemianopsia in one) after single-stage radiosurgery, but no patient developed a new permanent homonymous hemianopsia. Angiography was performed in all patients at a median of 26 months after

radiosurgery: 22 (65%) had complete obliteration, 10 (29%) had a significant decrease in AVM volume, one (3%) had only a persistent early draining vein without residual nidus, and one (3%) had no change in the AVM. Thirteen (81%) of 16 patients with AVMs less of than 4 ml had complete obliteration. Five patients had second-stage stereotactic radiosurgery after angiography revealed a persistent AVM nidus; two patients eligible for follow-up angiography had complete obliteration, thereby increasing the overall series obliteration rate to 71%. The calculated annual risk of AVM bleeding (before radiographic evidence of obliteration) was 2.4%. No patient bled after angiographically confirmed obliteration. In most patients stereotactic radiosurgery obliterates visual pathway AVMs and also preserves preoperative visual function. Multimodality management (embolization, microsurgery, or staged radiosurgery) enhances AVM obliteration and visual preservation rates.

106.

Year: 1996

Patient number: 99

Author: Tanaka, T.; Kobayashi, T.; Kida, Y.; Oyama, H.; Niwa, M.

Reference: Stereotactic and functional neurosurgery, 66, Suppl 1, 288-95, 1996

Title: Comparison between adult and pediatric arteriovenous malformations treated by Gamma Knife radiosurgery

Abstract: More than 290 cases of cerebral arteriovenous malformation have been treated at our hospital by Gamma Knife radiosurgery since May 1991, of which 99 were followed with angiography for 1 year or more. The results from adult and pediatric age groups were compared. There were 70 adults and 23 children. Previous hemorrhage had occurred in 73.7% of the adults and 91.3% of the children. The mean volume of the nidus was similar in both groups: 4.2 cm³ in adults and 4.8 cm³ in children. In both groups approximately 70% of the cases fell into Spetzler and Martin grade III. The mean margin dose was 20.0 Gy in the adults and 20.5 Gy in the children. Complete nidus occlusion at 1 year occurred in 45% of the adults and 74% of the children. The rates at 2 years were 81 and 94%, respectively. Complications occurred only in adults and consisted of 2 rebleeds, 1 radiation edema and 1 radiation necrosis. Gamma Knife radiosurgery is considered to be safer and have a higher success rate in children than in adults.

107.

Year: 1996

Patient number: 11

Author: Yamamoto, M.; Ide, M.; Jimbo, M.; Takakura, K.; Lindquist, C.; Steiner, L.

Reference: Surgical neurology, 45, 2, 110-9, 1996

Title: Neuroimaging studies of postobliteration nidus changes in cerebral arteriovenous malformations treated by gamma knife radiosurgery

Abstract: BACKGROUND: Following radiosurgical treatment, the majority of patients with arteriovenous malformations (AVMs) are periodically examined by means of computed

tomography (CT) and magnetic resonance imaging (MRI) to assess the attainment of nidus obliterations, as well as adverse radiation effects in the surrounding brain. However, few neuroimaging studies of the long-term results following complete obliterations, confirmed by angiography, have been published to date. **METHODS:** CT, MRI, magnetic resonance (MR) angiographic and angiographic images, obtained after angiographic confirmation of complete nidus obliteration, were reviewed in 11 AVM patients treated with gamma knife radiosurgery. The period between angiographic confirmation of nidus obliteration and these most recent examinations was 1284 months (mean, 29 months). **RESULTS:** In ten patients who were assessed by CT, the obliterated nidus was shown to be isodense (eight cases). A significant time-related decrease in contrast enhancement was observed within 1 to 2 postobliteration years (five/seven cases). Eight patients were evaluated by MRI. On T1-weighted imaging, the nidus was shown to be hypointense (six cases) or a mixture of hypointense and isointense areas (two cases). On T2-weighted imaging, nidus intensity varied more than than observed on T1-weighted imaging, and time-related intensity increases were observed (two/seven cases). No flow-signal void was demonstrated in any of these cases. In four of the seven cases, in which serial postobliteration follow-up MRI studies were conducted, significant gadolinium enhancement persisted 3 years or more after obliteration (maximum of 7 years). No vascular abnormalities were demonstrated in seven patients who were assessed by conventional angiography and/or MR angiography. **CONCLUSIONS:** Radiosurgery-induced changes in a nidus may continue for several years after angiography has shown complete AVM obliteration.

108.

Year: 1996

Patient number: 40

Author: Yamamoto, M.; Jimbo, M.; Hara, M.; Saito, I.; Mori, K.

Reference: Neurosurgery, 38, 5, 906-14, 1996

Title: Gamma knife radiosurgery for arteriovenous malformations: long-term follow-up results focusing on complications occurring more than 5 years after irradiation

Abstract: The detailed long-term follow-up results of 40 patients treated for cerebral arteriovenous malformations with gamma knife radiosurgery are presented, with special reference to postradiosurgical complications that can develop many years after irradiation. The follow-up period after radiosurgery was 54 to 205 months, excluding one mortality, with a mean and a median of 106 and 97 months, respectively. One patient (2.5%) has, to date, refused all neuroimaging follow-up examinations. Complete nidus obliteration was angiographically confirmed in 26 patients (65%) between 1 and 5 years after radiosurgery. In the remaining 13 patients (32.5%), although significant shrinkage of each nidus was angiographically demonstrated, complete obliteration was not attained during a 3- to 7-year period of follow-up after radiosurgery. Among these 13 patients, 1 underwent surgical extirpation of the nidus and 5 underwent second courses of gamma knife radiosurgery between 3 and 6 years after initial treatment; in 3 of the 5 patients, complete nidus obliteration was angiographically confirmed between 1 and 3 years after the second course of radiosurgery. There were no radiation- or arteriovenous malformation-related

mortalities. However, we did experience one angiography-related mortality. We also experienced one morbidity (probably caused by hemorrhagic stroke), which developed 5 years after 2-year postradiosurgical angiography had demonstrated complete obliteration, and three radiation-related morbidities, two of which (hemiparkinsonian syndrome and visual field disturbances caused by delayed cyst formation) occurred 5.5 and 7 years, respectively, after irradiation. Furthermore, we observed another two patients who, although asymptomatic to date, showed delayed cyst formation on magnetic resonance imaging 5 and 10 years after irradiation, respectively. In total, 3 (23%) of 13 patients who underwent computed tomography and/or magnetic resonance imaging more than 5 years after radiosurgery showed delayed cyst formation. In conclusion, long-term follow-up, particularly with the use of neuroimaging techniques, is necessary even after the treatment goal has been achieved.

109.

Year: 1995

Patient number: 14

Author: Abe, T.; Matsumoto, K.; Horichi, Y.; Hayashi, T.; Ikeda, H.; Iwata, T.

Reference: Neurologia medico-chirurgica, 35, 8, 580-3, 1995

Title: Magnetic resonance angiography of cerebral arteriovenous malformations

Abstract: Magnetic resonance (MR) angiography as a method for the long-term follow-up of cerebral arteriovenous malformations (AVMs) was assessed in 14 patients with cerebral AVMs. These patients were either untreated or treated with transarterial embolization and/or stereotactic radiosurgery (gamma knife). Two-dimensional- and three-dimensional (3D)-time-of-flight (TOF) techniques were useful for following AVMs with a small nidus and few feeders and drainers which were either untreated or had been treated only a few months previously. 3D-TOF MR angiography with a contrast agent was more useful for visualizing the vascular structure, including the residual nidus, during long-term follow-up of treated AVMs.

110.

Year: 1995

Patient number: 121

Author: Coffey, R. J.; Nichols, D. A.; Shaw, E. G.

Reference: Mayo Clinic proceedings, 70, 3, 214-22, 1995

Title: Stereotactic radiosurgical treatment of cerebral arteriovenous malformations
Gamma Unit Radiosurgery Study Group

Abstract: **OBJECTIVE:** To assess the role of clinical factors, size of lesion, site of involvement, and radiation dose in patients with cerebral arteriovenous malformations (AVMs) who underwent stereotactic radiosurgical treatment. **DESIGN:** We reviewed the results in 121 patients with cerebral AVMs treated with the Leksell Gamma Knife between January 1990 and December 1993 at the Mayo Clinic in Rochester, Minnesota. **MATERIAL AND METHODS:** The following strict dose- volume protocol was used: AVMs

2.0 cm or smaller in diameter (volume, 4.2 cm³ or less) received 20 Gy to the margin of the nidus, those between 2.1 and 3.0 cm in diameter (4.3 to 14.1 cm³) received 18 Gy to the margin, and those that exceeded 3.0 cm in diameter (more than 14.1 cm³) received 16 Gy to the margin. Lesions that involved the brain stem received a radiosurgical dose of 18 Gy or less to the margin. Patients participated in regular follow-up clinical and imaging studies for up to 55 months. **RESULTS:** Follow-up cerebral angiography in 43 patients demonstrated total obliteration of the AVM nidus in 31 (72.1%), including 5 of 7 (71.4%) who had AVMs with a volume larger than 10 cm³. Clinical follow-up revealed that 111 patients (91.7%) had a stable or improved outcome, 3 had a nonfatal AVM hemorrhage, 2 suffered a fatal hemorrhage, and 2 died of causes not directly attributed to the AVM or radiosurgical treatment. Two patients had new or increased, nondisabling neurologic deficits as a result of treatment, and one patient had a temporary partial eyelid ptosis. **CONCLUSION:** Our findings suggest that previous theories about the relationship between AVM size and rate of obliteration after radiosurgical treatment may need revision. Our experience confirms that radiosurgical treatment for cerebral AVMs is safe and effective, even in cases for which the latency period before obliteration is longer than 2 years.

111.

Year: 1995

Patient number: 14

Author: Guo, W. Y.; Pan, D. H.; Liu, R. S.; Chung, W. Y.; Shiau, C. Y.; Cheng, S. S.; Chang, C. Y.; Chen, K. Y.; Yeh, S. H.; Lee, L. S.

Reference: Stereotactic and functional neurosurgery, 64, Suppl 1, 258-69, 1995

Title: Early irradiation effects observed on magnetic resonance imaging and angiography, and positron emission tomography for arteriovenous malformations treated by Gamma Knife radiosurgery

Abstract: In 14 patients (7 males and 7 females, age 16-49, mean 29 years), medium-to-large arteriovenous malformations (AVMs; nidus volume 3.5-17.5 cm³, mean 9.4 cm³) were treated by Gamma Knife radiosurgery. Stereotactic MR and conventional angiography were included for targeting to improve targeting accuracy and tissue content in the irradiation volume. Maximum irradiation doses to the nidi were 36-40 Gy (mean 38.9 Gy) and minimum target doses were 18-24 Gy (mean 20 Gy).

112.

Year: 1995

Patient number: 15

Author: Lawton, M. T.; Hamilton, M. G.; Spetzler, R. F.

Reference: Neurosurgery, 37, 1, 29-35, 1995

Title: Multimodality treatment of deep arteriovenous malformations: thalamus, basal ganglia, and brain stem

Abstract: THE THERAPEUTIC APPROACH toward arteriovenous malformations (AVMs)

located in the basal ganglia, thalamus, and brain stem has evolved from microsurgical resection as the predominant therapy to a combination of microsurgery, embolization, and radiosurgery. This multimodality treatment was used in the management of 32 patients with deep AVMs of all sizes. Twenty-two patients with surgically accessible AVMs (i.e., typically located in the brain stem and thalamus) underwent microsurgical resection. The AVMs of half of these patients were devascularized preoperatively with transfemoral embolization. Five patients with residual AVMs were then treated with radiosurgery. Ten patients had AVMs, typically located in the basal ganglia, that were surgically inaccessible. These patients underwent embolization to reduce the AVM size, and the postembolization nidus was then treated with radiosurgery. For patients treated early in the series with a predominantly surgical approach, the complete resection rate was 43%. For patients treated later in the series after radiosurgery was incorporated into the management scheme, the complete elimination rate was 72%. Overall, there were no deaths in this series, and the permanent treatment-associated morbidity rate was 9%. These results indicate that an individualized, multimodality approach can be used to eliminate both large and small deep AVMs with an acceptably low morbidity and mortality rate.

113.

Year: 1995

Patient number: 24

Author: Mathis, J. A.; Barr, J. D.; Horton, J. A.; Jungreis, C. A.; Lunsford, L. D.; Kondziolka, D. S.; Vincent, D.; Pentheny, S.

Reference: AJNR. American journal of neuroradiology, 16, 2, 299-306, 1995

Title: The efficacy of particulate embolization combined with stereotactic radiosurgery for treatment of large arteriovenous malformations of the brain

Abstract: **PURPOSE:** To evaluate the efficacy of combined particulate embolization and single-stage stereotactic radiosurgery in the treatment of large arteriovenous malformations (AVMs) of the brain. **METHODS:** Twenty-four patients with large brain AVMs (diameter > 3.0 cm; volume > 14 cm³), who had previously undergone particulate embolization and stereotactic radiosurgery, were retrospectively evaluated 2 or more years after radiosurgery. **RESULTS:** In 12 (50%) of these patients there was complete AVM obliteration, comparing favorably with a 58% obliteration rate in a group of AVMs having a 4- to 10-cm³ volume, treated by radiosurgery alone. Recanalization of embolized, but not radiated, AVM segments was identified in 3 (12%) patients. However, long-term occlusion was demonstrated in the embolized portions of most AVMs subsequently treated by radiosurgery. Complications included 1 (4%) patient with a mild upper extremity paresis after radiosurgery and 2 (8%) patients with transient neurologic deficits after embolization. **CONCLUSION:** Combined embolization and stereotactic radiosurgery was more efficacious than radiosurgery alone for large brain AVMs. Recanalization after embolization did occur but was a relatively minor cause of treatment failure.

114.

Year: 1995

Patient number: 99

Author: Tanaka, T.; Kobayashi, T.; Kida, Y.; Oyama, H.; Niwa, M.

Reference: No shinkei geka, 23, 9, 773-7, 1995

Title: The comparison between adult and pediatric AVMs treated by gamma knife radiosurgery

Abstract: More than 290 cases of cerebral AVM had been treated by gamma knife radiosurgery since May, 1991, among which ninety-nine cases were angiographically followed up for at least one year. Comparison of the results between adult and pediatric AVMs were made. There were seventy six adult and twenty three child cases. Intracerebral hemorrhages in their past history were found in 73.7% of adult and 91.3% of child cases respectively, and the rate of intracranial hemorrhages in the pediatric group was higher than that in the adult group. The volume of the nidus of AVM in both groups was 4.2 ml in adults and 4.8 ml in children. Grade III of the Spetzler grading system occupied about 70% of all cases and was the most common grade in both groups. Treatment was performed with a mean marginal dose of 20.0Gy in adults and 20.5Gy in children. The complete occlusion of the nidus was obtained in 45% of the adult group and 74% of the pediatric group one year after, and in 81% and 95% respectively two years after the treatment was begun. As side effects, these were two rebleedings, one radiation necrosis and one radiation-induced edema in adults. However, no side effects were observed in children. It is considered that, when using gamma knife radiosurgery, pediatric AVMs are more likely to be occluded successfully and safely than adult AVMs.

115.

Year: 1995

Patient number: 14

Author: Wara, W.; Bauman, G.; Gutin, P.; Circillo, S.; Larson, D.; McDermott, M.; Sneed, P.; Verhey, L.; Smith, V.; Petti, P.; et al.

Reference: Stereotactic and functional neurosurgery, 64, Suppl 1, 118-25, 1995

Title: Stereotactic radiosurgery in children

Abstract: The role of stereotactic radiosurgery in the treatment of pediatric patients is still being explored. We report the Gamma Knife treatment of 33 patients under the age of 21, at the University of California, San Francisco, between the years 1991 and 1993. Treatment-related toxicity has been low. 10/14 patients treated for arteriovenous malformation (AVM) with follow-up > 1 month have shown partial or complete AVM obliteration. No patient has had a new hemorrhage after AVM treatment. In children with malignant tumors, treatment was well tolerated, although most patients, ultimately, had progressive disease. Stereotactic radiosurgery is logistically possible in the pediatric population. Its use in selected patients with AVMs seems appropriate, although its role in the treatment of malignant brain tumors remains to be defined.

116.

Year: 1995

Patient number: 121

Author: Yamamoto, Y.; Coffey, R. J.; Nichols, D. A.; Shaw, E. G.

Reference: Journal of neurosurgery, 83, 5, 832-7, 1995

Title: Interim report on the radiosurgical treatment of cerebral arteriovenous malformations The influence of size, dose, time, and technical factors on obliteration rate

Abstract: During the authors' initial 4-year experience with radiosurgery using the Leksell cobalt-60 gamma unit, they treated 121 patients with cerebral arteriovenous malformations (AVMs). The radiosurgical dose to the margin of the nidus was 20 Gy for lesions less than 2.0 cm in diameter (volume \leq 4.2 cm³); 18 Gy for malformations 2.1 to 3.0 cm in diameter (volume 4.2-14.1 cm³); and 16 Gy for malformations greater than 3.0 cm (volume $>$ 14.1 cm³). Fifty-one patients underwent follow-up angiography between 1 and 3 years after treatment, and complete obliteration of the nidus was confirmed in 38 (74.5%) of these patients. Thirty-two (74.4%) of 43 AVMs with volumes of 10 cm³ or less and six (75%) of eight larger AVMs (volume 11-30 cm³) showed complete obliteration. Analysis of the time course of AVM nidus shrinkage and obliteration showed that most of the radiosurgically induced effect had occurred by 36 months after treatment. Retrospective analysis of the dose plans for 10 AVMs that were not obliterated by 36 months after gamma knife radiosurgery at the authors' institution (eight cases) or elsewhere (two cases) revealed that six AVMs had not been covered completely by the prescribed isodose. Six (5%) of the 121 patients developed neurological deficits as a direct result of radiosurgical treatment. The authors infer from these data that malformations up to 30 cm³ in volume (approximately 4.0 cm in average diameter) can be treated effectively with an acceptably low complication rate using a radiosurgical dose of 16 Gy to the margin of the nidus. The obliteration rate for the larger malformations that were treated with a dose of 16 to 18 Gy appears to be similar to that for smaller ones treated with 18 to 20 Gy. As more experience accrues using radiosurgery to treat AVMs, patient selection criteria and the variables associated with successful obliteration of the nidus should become more clearly defined.

117.

Year: 1994

Patient number: 28

Author: Kondziolka, D.; Lunsford, L. D.; Kanal, E.; Talagala, L.

Reference: Neurosurgery, 35, 4, 585-90, 1994

Title: Stereotactic magnetic resonance angiography for targeting in arteriovenous malformation radiosurgery

Abstract: Because conventional stereotactic angiography provides only two-dimensional information for dose planning, we studied the accuracy and usefulness of stereotactic magnetic resonance angiography (sMRA) for arteriovenous malformation (AVM) radiosurgery in 28 consecutive patients. We hypothesized that the multidimensional data set provided by sMRA and the opportunity to image both blood vessels and brain

parenchyma would improve the accuracy of AVM irradiation and improve the safety of radiosurgery. Twenty-eight patients with AVMs in different brain locations and with a variety of AVM sizes (range, 15-31 mm mean diameter) had sMRA followed by stereotactic angiography. The sMRA images only were used to construct an initial radiosurgical plan. This plan was then used to outline the AVM volume defined by conventional angiography. In 24 patients, sMRA information equaled that of conventional angiography. In 3 patients, sMRA was better, because conventional angiography overestimated the size of the AVM nidus. In one patient, the conventional angiogram showed a second separate nidus (10-mm diameter) that was not as well defined on MRA. There were no complications with any procedure. In 16 patients (57%), sMRA provided critical information on AVM shape that was not provided by conventional angiography alone. Stereotactic MRA is a fast, noninvasive, inexpensive, multidimensional imaging method for AVM radiosurgery that provides information on vascular and parenchymal brain anatomy important for optimal dose planning. We believe that it can be used with confidence as the sole imaging method for medium- size, compact-nidus AVMs.

118.

Year: 1994

Patient number: 65

Author: Pollock, B. E.; Lunsford, L. D.; Kondziolka, D.; Maitz, A.; Flickinger, J. C.

Reference: Neurosurgery, 35, 1, 1-7, 1994

Title: Patient outcomes after stereotactic radiosurgery for operable arteriovenous malformations

Abstract: To define the outcomes after stereotactic radiosurgery performed for smaller volume arteriovenous malformations (AVMs) that are potentially suitable for surgical removal, we retrospectively reviewed our 4-year experience in 65 patients who declined microsurgery. All 65 patients had Spetzler-Martin Grade I or II AVMs and a minimum follow-up of 24 months (median, 29 mo). Symptomatic improvement after radiosurgery occurred in 52% of patients with seizures and in 63% of patients with headaches. The annual risk of AVM hemorrhage during the latency interval after radiosurgery was 3.7%. Five patients (7.7%) had a subsequent hemorrhage (all within 8 mo of radiosurgery); two died, and three recovered (one after hematoma evacuation and two with conservative management). Forty-seven patients (72%) returned to their previous employment status or activity level within 1 week of radiosurgery (92% within 1 yr). No patient suffered radiation-related complications. Twenty-seven (84%) of 32 patients evaluated by postradiosurgical angiography had complete AVM obliteration. Radiosurgery is an effective and less invasive management strategy for Grade I or II AVM patients who are either medically unsuitable for or unwilling to undergo surgical removal. The risk of AVM hemorrhage during the latency interval until obliteration occurs appears to be no different than the natural history of untreated AVMs. These results (including hemorrhage prevention and symptom amelioration) indicate that the conservative management of small AVMs can rarely be justified.

119.

Year: 1994

Patient number: 15

Author: Sakata, K.; Ishiwata, Y.; Hosoda, H.; Hidaka, T.; Yamataki, A.

Reference: Japanese Journal of Neurosurgery, 3, 2, 114-121, 1994

Title: An evaluation of ultrafast CT for planning the radiosurgical treatment of cerebral AVMs: Spatial evaluation of the nidus using dynamic CT with intraarterial bolus injection

Abstract: Radiosurgical dose planning for cerebral AVMs requires an accurate definition of the true tridimensional size and shape of the nidus. In this regard, it is difficult to define the accurate configuration of the nidus by conventional stereotactic angiography alone. However, as stereotactic information from axial imaging has an important role to play in obtaining true tridimensional information of the nidus, for investigating 15 cases with cerebral AVM, treated by Leksell gamma unit at Chigasaki Tokushukai Medical Center, the authors have performed dynamic CT (D-CT) using ultrafast CT (Imatron C-100) with an intraarterial bolus injection of a contrast material to delineate a more accurate configuration of the nidus on axial imaging. Further, the delineation of the nidus was also evaluated, especially the margin of the nidus in these images. In 12 of these 15 cases, D-CT clearly showed demarcated nidi. The margins of the nidi, however, were not clearly delineated in the remaining 3 cases, consisting of one case of an embolized AVM with polyvinyl alcohol, one case of a small AVM, and one postoperative case of feeder clipping. In 11 cases, we also compared the configuration of the nidus on axial imaging obtained by D-CT with that obtained by MRI. Demarcated nidi were clear in 10 of these cases (90.9%) by D-CT, and in 4 cases (36.4%) by MRI. In 7 cases, the definition of the margin of the nidus by MRI produced questionable results, because of hemosiderin (n = 3), gliosis and ischemic parenchyma (n = 2) and embolic material (n = 2). Because Imatron CT visualized sequential images of the contrast medium from the feeders through the drainers, each vascular component of the AVM could be distinguished in detail and the margin of the nidus on axial imaging was clearly defined in addition, it was also possible to analyze the AVM dynamics and define the true nidus by reviewing this information as recorded on the video tape. It thus was concluded that the dynamic CT using Imatron CT is very useful in planning radiosurgical treatment for AVMs and in some selected cases was found to be more reliable than MRI in accurately detecting the margin of the nidus.

120.

Year: 1994

Patient number: 37

Author: Tanaka, T.; Kobayashi, T.; Kida, Y.; Oyama, H.; Iwakoshi, T.

Reference: Japanese Journal of Neurosurgery, 3, 1, 24-28, 1994

Title: An assessment of stereotactic radiosurgery for treating arteriovenous malformations

Abstract: Stereotactic radiosurgery has been used to obliterate arteriovenous malformations (AVMs) and to judge the efficacy of this technique, follow-up angiography and magnetic resonance imaging (MRI) has been used to assess the results in AVM

patients given this therapy. Of 60 patients who received this therapy, angiography was used to follow the postoperative results in 37 patients for over a year. Twenty nine patients (78%) showed a good outcome, with 15 (40.5%) manifesting a complete obliteration and 14 (37.8%) a subtotal obliteration. The smaller the size of the nidus, the higher was the obliteration success. In those who showed a complete obliteration, the mean dose delivered to the AVM margin was 21.1 Gy. As for the effect of this therapy with respect to age, children showed higher obliteration rate than adults. Postoperative MRIs of 27 patients revealed radiation- induced edema in 8 (30%), and in only two of these 8 patients was this edema symptomatic. In those who showed radiation-induced edema, the mean dose delivered to the AVM margin was 19.8 Gy, the same dose that was given to the other patients. Based on these results, stereotactic radiosurgery was found to be a promising method to obliterate AVMs, especially those considered inoperable by other means.

121.

Year: 1993

Patient number: 28

Author: Duma, C. M.; Lunsford, L. D.; Kondziolka, D.; Bissonette, D. J.; Somaza, S.; Flickinger, J. C.

Reference: Acta neurochirurgica. Supplementum, 58, 92-7, 1993

Title: Radiosurgery for vascular malformations of the brain stem

Abstract: The challenges associated with microsurgery of vascular malformations located in the midbrain, pons and medulla have promoted the development of alternative therapeutic techniques. To assess the efficacy and safety of radiosurgery in the management of brain stem vascular malformations we reviewed our 5-year experience in 50 patients evaluated between 4 and 51 months (mean, 25 months) after radiosurgery. Twenty-eight patients (56%) underwent gamma unit radiosurgery for symptomatic arteriovenous malformations (AVMs), and 22 patients (44%) for angiographically occult vascular malformations (AOVMs). Patients varied in age from 7 to 76 years (mean, 39 years). Forty-one patients (82%) had from 1 to 5 hemorrhages prior to gamma knife radiosurgery. Ten (20%) had one or two prior unsuccessful operations, and 37 (74%) presented with a neurological deficit. Of the patients with AVMs, 6 were considered Spetzler Grade III, and 22 (79%) Grade VI (inoperable: major component within the brain stem parenchyma). Forty-four malformations (88%) were adjacent to or within the midbrain and pons; the remainder involved the medulla. Average malformation diameters varied from 6 to 30.4 mm (mean, 20.6; mean volume 4614 mm³). The minimal radiation dose to the margin of the malformations ranged from 12 to 25.6 Gy (mean, 18.9 Gy). Of the 28 patients with AVMs, 8 had follow-up angiograms at a minimum of 2-years after radiosurgery (or sooner if their MRIs suggested obliteration). Of these patients, 7 (88%) showed complete obliteration of their malformations. No patients with AOVMs rehemorrhaged if more than 15 months elapsed after radiosurgery. (ABSTRACT TRUNCATED AT 250 WORDS).

122.

Year: 1993

Patient number: 191

Author: Forster, D. M.; Kunkler, I. H.; Hartland, P.

Reference: Stereotactic and functional neurosurgery, 61, Suppl 1, 20-2, 1993

Title: Risk of cerebral bleeding from arteriovenous malformations in pregnancy: the Sheffield experience

Abstract: Data were obtained from 191 women with cerebral arteriovenous malformations (AVMs) referred for stereotactic radiosurgery with the Leksell Gamma Unit in Sheffield. The risk of cerebral bleeding from arteriovenous malformations during pregnancy was examined and related to the different trimesters of pregnancy in these women. Some tentative guidelines are suggested for advising women with AVMs, who become pregnant.

123.

Year: 1993

Patient number: 816

Author: Guo, W. Y.

Reference: Acta radiologica. Supplementum, 388, 1-34, 1993

Title: Radiological aspects of gamma knife radiosurgery for arteriovenous malformations and other non-tumoural disorders of the brain

Abstract: The aims of the thesis were to investigate stereotaxic procedures in radiosurgery for cerebral arteriovenous malformations (AVMs) and radiation effects of single session high-dose irradiation delivered by gamma knife on the human brain. Investigation of gamma knife radiosurgery in 1,464 patients constitutes the data base of this thesis. High quality stereotaxic angiography is the gold standard targeting imaging in radiosurgery for cerebral AVMs, particularly for small AVMs or residual AVMs after other treatments. For medium and large size AVMs, stereotaxic MR techniques can improve targeting precision and decrease irradiation volume as compared to stereotaxic angiography in selected cases provided that proper pulse sequences are used. Combined treatments, where embolization precedes radiosurgery, can improve amenability of the treatment for large AVMs. This is on condition that the partially embolized nidi are well delineated and the volume of the residual nidi has been decreased to a level where an optimum irradiation can be safely prescribed. Radiologically, adverse radiation effects (ARE) of gamma knife radiosurgery for cerebral AVMs are observed in 16% (131/816) of the patients. The ARE are observed as a focal low attenuation on CT or as a focal high signal on MR image without enhancement in 47% (61/131), and as a peripheral or homogeneous enhancing lesion in 48% (63/131). MR imaging is more sensitive than CT in detecting the ARE. 91% of the ARE are observed within 18 months after radiosurgery and 89% are seen to regress within 18 months. Clinically, symptomatic ARE are only observed in 6% (51 /816) and only in half of them, i.e. 3%, are the symptoms permanent. The risk of ARE in radiosurgery for venous angiomas is higher as compared to AVMs. Other mechanisms have probably been

employed. In gamma capsulotomy, the necrotic lesions and reaction volumes created by using multiple isocentres of 4 mm collimators are less predictable as compared to that by single isocentre. Volume effects and depreciation of the steep isodose gradient are hypothesised as the leading factors of the inconsistency. Based on the in vivo assessment of the radiation effects observed on the basically normal human brain it is concluded that irradiation volume is strongly related to the radiation effects and is one of the important considerations in decision making for radiosurgery. Volume of brain tissue exposed to irradiation could be minimised and precision of targeting could be maximised provided that a proper stereotaxic imaging is used.(ABSTRACT TRUNCATED AT 400 WORDS).

124.

Year: 1993

Patient number: 18

Author: Guo, W. Y.; Lindquist, C.; Karlsson, B.; Kihlström, L.; Steiner, L.

Reference: International journal of radiation oncology biology physics, 25, 2, 315-23, 1993

Title: Gamma knife surgery of cerebral arteriovenous malformations: serial MR imaging studies after radiosurgery

Abstract:PURPOSE: To investigate the temporal sequence of post radiosurgery magnetic resonance imaging changes in cerebral arteriovenous malformations.

METHODS AND MATERIALS: Eighteen patients were regularly followed up after gamma knife surgery. The follow-up intervals ranged from one day to 44 months. High signal lesion in or around arteriovenous malformations on T2-weighted magnetic resonance images corresponding to the treatment volume and developing after radiosurgery were defined as the adverse reaction of the irradiation. This high signal and the regression of arteriovenous malformations nidus after radiosurgery were evaluated. **RESULTS:** Adverse reaction of irradiation was observed in nine cases. Seven of them were symptomatic. The reactions presented as focal high signal in three cases and focal high signal with extension along the neural tracts in six cases. The reactions were seen either immediately after treatment (one case), between 3 and 14 months (seven cases), and 40 months after treatment (one case). The regression of the adverse reaction was observed to start 5 +/- 3 months after its appearance. Regression of the arteriovenous malformations' nidus was found in 16 cases. In two cases the AVMs became invisible on magnetic resonance images but the angiogram still demonstrated abnormal shunts. In another one case with angiogram showing total obliteration, the nidus was erroneously interpreted as incomplete obliteration on magnetic resonance images. **CONCLUSION:** It is concluded that magnetic resonance imaging is a sensitive in vivo method for detecting cerebral radiation injury. Magnetic resonance imaging offers a method for evaluating the regression of arteriovenous malformations' nidus, but the diagnosis of complete obliteration of the nidus after radiosurgery still relies on the angiogram.

125.

Year: 1993

Patient number: 46

Author: Guo, W. Y.; Wikholm, G.; Karlsson, B.; Lindquist, C.; Svendsen, P.; Ericson, K.

Reference: Acta radiologica, 34, 6, 600-6, 1993

Title: Combined embolization and gamma knife radiosurgery for cerebral arteriovenous malformations

Abstract: In a study of 46 patients with cerebral arteriovenous malformations (AVMs) the value of combining embolization and gamma knife radiosurgery was assessed. In 35 patients with large grade III to V AVMs (Spetzler-Martin system) staged combined treatment was planned. In 11 patients, radiosurgery complemented embolization for a residual AVM. The number of embolization sessions ranged from 1 to 7 (median 2). Twenty-six patients needed multiple embolization sessions. In 28 patients the grade of AVMs decreased as a result of embolization. In 16 patients collateral feeding vessels developed after embolization which made delineation of the residual nidus difficult. The time lag between the last embolization and radiosurgery ranged from 1 to 24 months (median 4). Nineteen of 35 large grade III to V AVMs were possible to treat by radiosurgery following embolization. In the 46 patients complications occurred in 9 from embolization and in 2 from radiosurgery. Two patients had transient and 9 had permanent neurologic deficits. It is concluded that embolization facilitates radiosurgery for some large AVMs and therefore this combined treatment has a role in the management of AVMs.

126.

Year: 1993

Patient number: 22

Author: Yamamoto, M.; Jimbo, M.; Ide, M.; Lindquist, C.; Steiner, L.

Reference: Surgical neurology, 40, 6, 485-90, 1993

Title: Postradiation volume changes in gamma unit-treated cerebral arteriovenous malformations

Abstract: Postradiation changes in angiographically determined nidus volume were quantitatively studied in 22 arteriovenous malformation (AVM) cases treated by gamma unit radiosurgery. The postradiosurgical decrease was statistically significant by post-treatment year 2 ($p < .05$). In children, AVMs tended to be obliterated more quickly than in adults. Volume reduction was more rapid in nidi receiving 25 Gy or more than in those receiving less than 25 Gy ($p < .01$). However, there were no significant differences in nidus volume decrease between these two dose groups at the second or third postradiosurgical year. Dose response curves were obtained 1, 2, and 3 years following treatment.

127.

Year: 1992

Patient number: 72

Author: Flickinger, J. C.; Lunsford, L. D.; Kondziolka, D.; Maitz, A. H.; Epstein, A. H.; Simons, S. R.; Wu, A.

Reference: International journal of radiation oncology biology physics, 23, 1, 19-26, 1992

Title: Radiosurgery and brain tolerance: an analysis of neurodiagnostic imaging changes after gamma knife radiosurgery for arteriovenous malformations

Abstract: In order to analyze complications and the factors responsible for the development of serial imaging changes after stereotactic radiosurgery for intracranial arteriovenous malformations, we reviewed serial post-treatment magnetic resonance imaging scans in 72 patients. Median follow-up was 23 months (range 12 to 35 months). Twenty patients developed post-radiosurgical imaging changes consisting of new regions of increased T2 signal on magnetic resonance imaging in brain surrounding the arteriovenous malformation (two year actuarial incidence of 31%). Imaging changes were associated with headache or new neurological deficits in nine of these 20 (45%) and remained asymptomatic in 11 (55%). Symptoms developed in three of 13 patients with imaging changes in the cerebral cortex or cerebellum, in contrast to six of seven patients who had symptoms with imaging changes in the brainstem ($p = .028$). The onset of imaging changes varied from five to 18 months after radiosurgery (median, 12 months). Serial follow-up scans four to 25 months after the onset of imaging changes were available for review in 16 patients. Post-radiosurgical imaging changes completely resolved within 4 to 19 months in ten patients and have not yet completely resolved after 6 to 25 months in six patients. The projected actuarial rate for resolution of imaging changes was 88%, 19 months after onset; the median time for resolution was 14 months. Univariate analysis revealed that the development of imaging changes was significantly associated with treatment volume ($p = .025$), the risk predicted from the integrated logistic formula ($p = .042$), and the number of isocenters treated ($p = .042$). In multivariate analysis, volume was the only factor significantly associated with the development of imaging changes.

128.

Year: 1992

Patient number: 251

Author: Lunsford, L. D.; Kondziolka, D.; Bissonette, D. J.; Maitz, A. H.; Flickinger, J. C.

Reference: Neurosurgery clinics of North America, 3, 1, 79-98, 1992

Title: Stereotactic radiosurgery of brain vascular malformations

Abstract: Stereotactic radiosurgery using the gamma unit was performed in 251 patients with brain vascular malformations in a 3-year interval. Our efforts include the identification of factors related to both success and complications, including analysis of the malformation location, volume, and dose used. Radiosurgery is a valuable alternative treatment for many patients with brain vascular malformations, including those currently believed to be poor surgical candidates.

129.

Year: 1992

Patient number: 247

Author: Steiner, L.; Lindquist, C.; Adler, J. R.; Torner, J. C.; Alves, W.; Steiner, M.

Reference: Journal of neurosurgery, 77, 1, 1-8, 1992

Title: Clinical outcome of radiosurgery for cerebral arteriovenous malformations

Abstract:The clinical outcomes are described for 247 consecutive cases of arteriovenous malformation (AVM) treated with the gamma knife between April, 1970, and December 31, 1983. Headache resolved in 65 (66.3%) of the 98 patients presenting with this symptom and improved in an additional nine (9.2%). Of 59 patients admitted with seizures, 11 (18.6%) became seizure-free without anticonvulsant medication and an additional 30 patients (50.8%) became seizure-free with anticonvulsant medication. Pre-existing neurological deficits improved or totally disappeared following radiosurgery in 56.7% of affected cases. This improvement presumably occurred within the frame of the natural history. The protective effect of the ionizing beams against hemorrhage in incompletely obliterated AVM's is analyzed. To assess the rate of rebleeding, probability estimates were calculated using both the person-year method and the Kaplan-Meier life table. With the person-year method the actual rebleed rate is not too different from the values observed in the natural history of the disease (2% to 3% /yr). Analysis by Kaplan-Meier life-table estimates demonstrated a risk of nearly 3.7%/yr until 60 months after radiosurgery. Five years following treatment, the life table ends in a plateau which could be interpreted as an indication of decrease in the risk of hemorrhage. However, long flat regions at the right end of the life table do not imply that the real risk of rebleeding is negligible unless a large number of patients have been followed well into or beyond the flat region.

130.

Year: 1992

Patient number: 160

Author: Sutcliffe, J. C.; Forster, D. M.; Walton, L.; Dias, P. S.; Kemeny, A. A.

Reference: British journal of neurosurgery, 6, 3, 177-85, 1992

Title: Untoward clinical effects after stereotactic radiosurgery for intracranial arteriovenous malformations

Abstract:Stereotactic radiosurgery has become one of the most acceptable means of treating deep-seated intracranial arteriovenous malformations, as well as being a useful adjunct in a number of other pathologies. One hundred and sixty patients are discussed, having follow-up of at least 2 years. Radionecrosis occurred in six patients and haemorrhage in the latent period prior to thrombo-obliteration in a further six. Successful thrombo-obliteration was ultimately achieved in 76% of patients. As a bonus, epilepsy was improved in 29 of 48 patients presenting with seizures and worsened transiently in only three of these.

131.

Year: 1992

Patient number: 25

Author: Yamamoto, M.; Jimbo, M.; Kobayashi, M.; Toyoda, C.; Ide, M.; Tanaka, N.; Lindquist, C.; Steiner, L.

Reference: Surgical neurology, 37, 3, 219-30, 1992

Title: Long-term results of radiosurgery for arteriovenous malformation: neurodiagnostic imaging and histological studies of angiographically confirmed nidus obliteration

Abstract: Detailed follow-up results for 25 patients treated for cerebral arteriovenous malformation (AVM) with a gamma unit are presented. Complete nidus obliteration was angiographically confirmed in 16 (73%) of 22 cases receiving full-dose irradiation. There were no radiation- or AVM-related mortalities. However, we did experience one case of radiation-related morbidity and one of angiography-related mortality, the autopsy findings of which are discussed. Computed tomography scan and magnetic resonance imaging follow-up studies of radiosurgically treated AVMs indicated that increased enhancement of the nidus after contrast or gadolinium administration could persist even after obliteration of the AVM was angiographically confirmed.

132.

Year: 1991

Patient number: 227

Author: Lunsford, L. D.; Kondziolka, D.; Flickinger, J. C.; Bissonette, D. J.; Jungreis, C. A.; Maitz, A. H.; Horton, J. A.; Coffey, R. J.

Reference: Journal of neurosurgery, 75, 4, 512-24, 1991

Title: Stereotactic radiosurgery for arteriovenous malformations of the brain

Abstract: Stereotactic radiosurgery successfully obliterates carefully selected arteriovenous malformations (AVM's) of the brain. In an initial 3-year experience using the 201-source cobalt-60 gamma knife at the University of Pittsburgh, 227 patients with AVM's were treated. Symptoms at presentation included prior hemorrhage in 143 patients (63%), headache in 104 (46%), and seizures in 70 (31%). Neurological deficits were present in 102 patients (45%). Prior surgical resection (resulting in subtotal removal) had been performed in 36 patients (16%). In 47 selected patients (21%), embolization procedures were performed in an attempt to reduce the AVM size prior to radiosurgery. The lesions were classified according to the Spetzler grading system: 64 (28%) were Grade VI (inoperable), 22 (10%) were Grade IV, 90 (40%) were Grade III, 43 (19%) were Grade II, and eight (4%) were Grade I. With the aid of computer imaging-integrated isodose plans for single- treatment irradiation, total coverage of the AVM nidus was possible in 216 patients (95%). The location and volume of the AVM were the most important factors for the selection of radiation dose. Magnetic resonance (MR) imaging was performed at 6-month intervals in 161 patients. Seventeen patients who had MR evidence of complete obliteration underwent angiography within 3 months of imaging: in 14 (82%) complete obliteration was confirmation being 4 months (mean 17 months) after radiosurgery. The 2-year obliteration rates according to volume were: all eight (100%) AVM's less than 1 cu cm; 22 (85%) of 26 AVM's of 1 to 4 cu cm; and seven (58%) of 12

AVM's greater than 4 cu cm. Magnetic resonance imaging revealed postirradiation changes in 38 (24%) of 161 patients at a mean interval of 10.2 months after radiosurgery; only 10 (26%) of those 38 patients were symptomatic. In the entire series, two patients developed permanent new neurological deficits believed to be treatment-related. Two patients died of repeat hemorrhage at 6 and 23 months after treatment during the latency interval prior to obliteration. Stereotactic radiosurgery is an important method to obliterate AVM's, especially those previously considered inoperable. Success and complication risks are related to the AVM location and the volume treated.

133.

Year: 1990

Patient number: 161

Author: Coffey, R. J.; Lunsford, L. D.; Bissonette, D.; Flickinger, J. C.

Reference: Stereotactic and functional neurosurgery, 54, 535-40, 1990

Title: Stereotactic gamma radiosurgery for intracranial vascular malformations and tumors: report of the initial North American experience in 331 patients

Abstract: We reviewed the initial experience with 331 consecutive patients treated during the first 2 years of operation of the University of Pittsburgh Gamma Unit. Among 178 patients with vascular malformations, 161 had angiographically demonstrable arteriovenous malformations, and 17 had angiographically occult malformations. Patients with tumors included 123 with histologically benign, predominantly extra-axial neoplasms and 30 with malignant, predominantly intra-axial neoplasms. When the arteriovenous malformation nidus could be covered with at least the 50% isodose line and a dose to the margin greater than or equal to 20 Gy, 60% were obliterated within 1 year. Patients with benign tumors and well-circumscribed malignant tumors did not experience tumor growth within the radiosurgical treatment volume. The role of radiosurgery is expanding to include primary treatment of larger lesions than was formerly possible and adjunctive treatment of more complex arteriovenous malformation and tumors.

134.

Year: 1990

Patient number: 113

Author: Lunsford, L. D.; Flickinger, J.; Coffey, R. J.

Reference: Archives of neurology, 47, 2, 169-75, 1990

Title: Stereotactic gamma knife radiosurgery Initial North American experience in 207 patients

Abstract: The first North American gamma knife for stereotactic radiosurgery of brain tumors and arteriovenous malformations entered the therapeutic armamentarium at the University of Pittsburgh (Pa) on August 14, 1987. In this article, we report our initial testing and subsequent experience with this technique. In the first 16 months of operation, 207 patients were treated (113 had arteriovenous malformations, 78 had extra-axial skull base neoplasms, 9 had glial neoplasms, and 7 had metastatic tumors). The patients'

lesions either were considered previously as inoperable or were residual lesions after attempted surgical resection, or the radiosurgery was performed after the patient declined surgical excision. Gamma radiosurgery was associated with no surgical mortality and no significant early morbidity, and the results were encouraging during the minimum follow-up period of 6 months. Compared with treatment by conventional intracranial surgery (craniotomy), both the average length of stay and hospital charges for radiosurgery were significantly lower. Our initial experience further suggests that stereotactic radiosurgery using the gamma knife is a therapeutically effective and economically sound alternative to microneurosurgical removal of selected intracranial tumors and vascular malformations.

135.

Year: 1989

Patient number: 18

Author: Altschuler, E. M.; Lunsford, L. D.; Coffey, R. J.; Bissonette, D. J.; Flickinger, J. C.

Reference: Pediatric neuroscience, 15, 2, 53-61, 1989

Title: Gamma knife radiosurgery for intracranial arteriovenous malformations in childhood and adolescence

Abstract: Eighteen children or adolescents with intracranial arteriovenous malformations (AVM) underwent stereotactic radiosurgery using the first North American gamma knife. This closed-skull, single-treatment therapy, utilizing 201 ionizing beams of gamma-irradiation, was used as an alternative to microsurgical removal in these selected patients (aged 34 months to 18 years, mean 12.3 years) beginning in August 1987. No significant perioperative morbidity occurred, and no patient rebled or died in the follow-up interval ranging between 7 and 19 months. Computed tomography (CT) and magnetic resonance imaging (MRI) were used to monitor the response to treatment and to determine when postoperative angiography was indicated. Of seven AVMs examined with cerebral angiography 1 year after treatment, three were completely obliterated; three others were significantly smaller, and their complete obliteration is anticipated by 2 years after treatment. Follow-up CT or MRI confirmed attenuation or signal changes suggestive of edema surrounding the treatment volume in 3 patients; 1 had transient worsening of a preexisting neurological deficit. Although a more long-term perspective is still required for this new technology now available in the United States, we believe that gamma knife stereotactic radiosurgery is a safe and effective method to obliterate AVM deemed too risky for microsurgical removal.

136.

Year: 1989

Patient number: 52

Author: Kemeny, A. A.; Dias, P. S.; Forster, D. M.

Reference: Journal of neurology neurosurgery and psychiatry, 52, 5, 554-8, 1989

Title: Results of stereotactic radiosurgery of arteriovenous malformations: an analysis of

52 cases

Abstract:The stereotactic radiosurgery unit in Sheffield became operational in September 1985 and over 180 patients harbouring AVMs have been treated. The first 52 patients underwent one year follow up angiography and comprise the material for this study. At one year 26 patients (50%) already had a favourable outcome (16 complete and 10 almost complete obliteration). The results were the same in the two sexes. There was a better response in younger patients: under 20 years 75% favourable, between 20 and 40 years 45% favourable and above 40 years about 25% favourable. Malformations in a lateral position appeared to respond better than those in the midline. Lesions fed by vessels from more than one large vessel territory had less chance of complete obliteration at one year than those gaining blood from only one main supply. There was no difference in outcome between small malformations (less than 2 cm³) medium (2-3 cm³) or large (greater than 3 cm³). No immediate morbidity or late side effects were encountered in these patients. Stereotactic radiosurgery is a safe and effective method in the treatment of arteriovenous malformations but there is a relatively long latency. The number of malformations obliterated is expected to be much higher when two years have elapsed after treatment.

137.

Year: 1989

Patient number: 29

Author: Lunsford, L. D.; Flickinger, J.; Lindner, G.; Maitz, A.

Reference: Neurosurgery, 24, 2, 151-9, 1989

Title: Stereotactic radiosurgery of the brain using the first United States 201 cobalt-60 source gamma knife

Abstract:The first United States 201 cobalt-60 source gamma knife for stereotactic radiosurgery of brain tumors and arteriovenous malformations became operational at the University of Pittsburgh on August 14, 1987. Four and one-half years of intensive planning, regulatory agency review, and analysis of published results preceded the first radiosurgical procedure. Installation of this 18,000-kg device and loading of the 201 cobalt-60 sources posed major challenges in engineering, architecture, and radiophysics. In the first 4 months of operation, we treated 52 patients (29 with arteriovenous malformations, 19 with extra-axial neoplasms of the skull base, and 4 with intra-axial malignant tumors). Most patients either had lesions considered inoperable or had residual lesions after attempted surgical resection. Neither surgical mortality nor significant morbidity was associated with gamma knife radiosurgery. As compared with treatment by conventional intracranial surgery (craniotomy), the average length of stay for radiosurgery was reduced by 4 to 14 days, and hospital charges were reduced by as much as 65%. Based on both the previously published results of treatment of more than 2,000 patients worldwide and on our initial clinical experience, we believe that gamma knife stereotactic radiosurgery is a therapeutically effective and economically sound alternative to more conventional neurosurgical procedures, in selected cases.