Three-dimensional angiography for radiosurgical treatment planning for arteriovenous malformations

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Object. Radiosurgical treatment of a cerebral arteriovenous malformation (AVM) requires the precise definition of the nidus of the lesion in stereotactic space. This cannot be accomplished using simple stereotactic angiography, but requires a combination of stereotactic biplanar angiographic images and stereotactic contrast-enhanced computerized tomography (CT) scans. In the present study the authors describe a method in which three-dimensional (3D) rotational angiography is integrated into stereotactic space to aid treatment planning for radiosurgery.

Methods. Twenty patients harboring AVMs underwent treatment planning prior to linear accelerator radiosurgery. Planning involved the acquisition of two different data sets, one of which was obtained using the standard method (a combination of biplanar stereotactic angiography with stereotactic CT scanning), and the other, which was procured using a new technique (nonstereotactic 3D rotational angiography combined with stereotactic CT scanning by a procedure of image fusion).

The treatment plan that was developed using the new method was compared with that developed using the standard one. For each patient the number of isocenters and the dimension of selected collimators were the same, based on the information supplied in both methods. Target coordinates were modified in only five cases and by a limited amount (mean 0.7 mm, range 0.3–1 mm).

Conclusions. The new imaging modality offers an easier and more immediate interpretation of 3D data, while maintaining the same accuracy in target definition as that provided by the standard technique. Moreover, the new method has the advantage of using nonstereotactic 3D angiography, which can be performed at a different site and a different time with respect to the irradiation procedure.

Key Words • arteriovenous malformation • stereotactic radiosurgery • three-dimensional angiography

Single-session, stereotactically focused irradiation (radiosurgery) is considered a treatment alternative for selected cerebral AVMs. The progressive obliteration of nidus vessels induced by a high radiation dose has proved to be equally safe and effective, regardless of the device used: gamma knife, cyclotron, or adapted linear accelerator.10,11,13,19,23,24 No matter which device is used, the success rate of radiosurgery, in terms of complete obliteration of the nidus, depends mainly on an accurate 3D reconstruction of the target, the AVM nidus. Since early reports on radiosurgery, stereotactic angiography has been considered to be the main imaging database for precise AVM delineation.10,23 Conventional stereotactic angiography is limited in its definition of AVM margins, however, especially in the case of irregularly shaped nidi.13,17 Adequate treatment plans are based on angiographic data that are integrated with spatial information provided by 3D CT and/or MR imaging examinations.7,13,18–20

Recently, a new neuroradiological procedure, which presents a reconstructed 3D image of intracranial vessels (3D rotational angiography) has been introduced to clinical practice and found to be superior in delineating cerebral AVMs.3,6,16 The aim of this report is to present a new method for using 3D rotational angiography for radiosurgical treatment planning and to compare the results achieved with those obtained using the standard technique, which is based on the combination of stereotactic angiography and CT scanning.

Clinical Material and Methods

From December 2001 to June 2002, 20 patients (nine male and 11 female patients) affected by cerebral AVMs were treated with radiosurgery at our institution. The ages of the patients ranged from 11 to 62 years (mean 32.4 years). At presentation the symptoms included bleeding in 10 patients, epilepsy in four, neurological symptoms in four, and headache in two patients. Before radiosurgery, two patients underwent attempts at surgical removal of the lesion, and three patients underwent incomplete AVM embolization. The maximum dimension of the AVM nidi ranged

Abbreviations used in this paper: AVM = arteriovenous malformation; CT = computerized tomography; MR = magnetic resonance; TPS = treatment planning system; 3D = three-dimensional.
Three-dimensional angiography for radiosurgery

from 7 to 32 mm (mean 16.3 mm), and the estimated volume of the target ranged from 171 to 7812 mm³ (mean 2047 mm³). A radiation dose between 24 and 29 Gy (mean 28.2 Gy) was delivered to the isocenter in a single session. The borders of the target volume encompassed 60 to 90% isodose surfaces. One isocenter with circular collimators ranging from 6 to 25 mm was selected in 12 patients, whereas in eight patients two or three isocenters were selected. The same procedure was repeated in the whole series of 20 patients.

In each patient, treatment planning was performed using two different techniques.

**Standard Technique**

After fixation of the Cosman-Roberts-Wells head frame and the angiographic localizer (Radionics, Inc., Burlington, MA), a complete stereotactic digital subtraction angiography study was performed. The anteroposterior and lateral projections that are relevant for delineation of the nidus of an AVM were elaborated for adequate correction of distortion that is characteristic of digitally subtracted angiograms. Selected images were printed after this correction. The angiographic localizer was then replaced by the CT localizer. A contrast-enhanced CT study was performed and recorded, and the images were sent to a TPS (Pinnacle³, Philips Medical Systems, Best, The Netherlands). The treatment planning procedure consisted of a reconstruction of the AVM nidus based on the CT data; angiograms were acquired by digitizing the printed stereotactic angiographic images. Radiosurgical treatment planning was then performed in the usual manner: definition of the target volume with the aid of the CT and angiographic data; calculation of the stereotactic coordinates of the isocenter(s); selection of the collimator(s); and determination of the dose of radiation to be delivered.

**The 3D Angiography Technique**

Before head frame fixation, a nonstereotactic 3D rotational angiography study (Philips Integris Allura; Philips Medical Systems) was performed while the radiation source and detectors were rotating 240° around the patient’s head; the rotation lasted 4 seconds, during which 100 frames were acquired. Different angiographic phases could be studied by modifying the time at which the contrast was injected with respect to the C-arm rotation. The 3D reconstruction was based on images corrected for inherent distortion. The efficiency of the correction algorithm was previously evaluated in both geometric and anthropomorphic phantoms, and found to be accurate and reliable, confirming data that have already been published. Although the manufacturers’ specifications are less restrictive, we did not find discrepancies greater than 1 mm in the lengths of the calibration rods (1–15 cm) positioned at the center and margins of the reconstructed volume. Three rods were oriented orthogonally to each other, so that regional spatial distortion in the field of view could be easily detected. Measurements were performed by the TPS (Pinnacle³, which “read” the coordinates of the rod ends and calculated their distances. A stereotactic head phantom (Radionics, Inc.) was used for confirmation of spatial accuracy. The phantom consists of a human skull containing four different geometric test objects (cylinder, cone, sphere, and cube), the positions and dimensions of which are known a priori. The phantom was scanned by rotational angiography and the dimensions and relative position of each object were measured. Eight geometric elements (lengths and distances) were identified as indices of quality: discrepancies in a series of five measurements of the eight elements (40 measurements) ranged from 0 to 1.4 mm (mean 0.4 mm). There was no dependence on direction for the observed errors, as would be expected considering the cubic shape of the voxels (0.7 × 0.7 × 0.7 mm) used in rotational angiography.

Radiosurgical treatment planning was performed using the Pinnacle³ TPS. The complete angiographic 3D data set was converted into a format compatible with the TPS by using commercially available software (DCMView, Tecnologie Avanzate T.A. Srl, Torino, Italy). The data were read as a series of 256 nonsubtracted coronal slices, each one with a 256 × 256 resolution. The main database consisted of the stereotactic contrast-enhanced CT studies that had previously been performed and recorded.

**Image Fusion**

The 3D angiograms were located in stereotactic space by applying an iterative manual procedure of image fusion based on rigid body transformation.

Because the reconstructed volume was a cylinder measuring approximately 18 cm in diameter (using a 30-cm diameter image intensifier), no external stereotactic localizers were used in the fusion process, which has to be based only on anatomical details.

The same head phantom used to test the spatial accuracy of 3D angiography was used to verify the accuracy of the image fusion procedure. Singular points in the four test objects were identified; the stereotactic coordinates of these points are known a priori. The head phantom was scanned by CT (with head frame and stereotactic localizers), leaving only one geometric test object in position (the reference object), and by 3D rotational angiography (without stereotactic localizers) with all four test objects in place. The data set provided by 3D angiography was fused with that provided by the stereotactic CT study, relying on bone details and the contours of the only test object present in both examinations—the reference test object. The stereotactic coordinates of identified points that were visible in the nonstereotactic 3D angiography, but invisible in the stereotactic CT scan, were determined on the image fusion data set and compared with known values. We calculated the coordinates of three to five points of the CT-invisible test objects in four sets of fused images, each one based on a different reference test object. In all, the x, y, and z coordinates of 15 points were calculated. Differences ranged from 0.2 to 1.6 mm (mean 0.6 mm).

In clinical practice, for each patient, the bone details were used to achieve an initial alignment, which is refined also by means of soft tissue and, in particular, anatomical details of intracranial vessels. The two data sets were initially aligned using translation and rotation steps to achieve a satisfactory coincidence of bone profiles in the midline sagittal plane. Other parallel planes were subsequently verified and adjustments were made if necessary. In the following step, coronal bone images were made to coincide and, finally, axial slices were examined and corrected if needed. The whole procedure was then repeated, starting again from...
the sagittal orientation, until a satisfactory result was obtained for the bone structures. Vessels visible on both CT scans and angiograms were then examined for coincidence; further adjustments were made, if necessary, for detailed matching of more prominent vascular structures in the region of the AVM to be treated (feeding arteries and draining veins). The accuracy of the match was verified for each patient and involved a detailed comparison along an arbitrary planar reconstruction. The whole fusion procedure takes approximately 10 to 45 minutes. The fusion produces the alignment of the nonstereotactic angiography volume to the stereotactic CT scan volume. The result is a new data set consisting of angiograms that are related to CT-derived stereotactic fiducial markers; in this new data set it is possible to perform stereotactic localization and radiosurgical treatment planning.

The time sequence of the procedure was as follows: a frameless 3D rotational angiography study was performed and recorded, and its data format was converted. Subsequently, after frame fixation, a standard biplane stereotactic angiography study was undertaken. Adequate angiographic pictures for targeting and correction of digital distortion were selected in the following step. Meanwhile, a contrast-enhanced CT scan was obtained and sent to the appropriate TPS (XKnife [Radionics, Inc.] for the standard procedure and Pinnacle’ TPS for image fusion and the 3D procedure).

Treatment planning was always performed by the senior author, a neurosurgeon (F.C.), with the assistance of the
medical physicist and the neuroradiologist. The standard technique of treatment planning was performed first: the appropriate coordinates of the target(s), collimator dimensions, and beam geometry were selected. The same radiosurgery team then moved to the 3D system. First, fusion of the images provided by 3D rotational angiography and stereotactic CT scanning was performed. Second, treatment planning was undertaken and the results that were obtained using the 3D method were compared with those already obtained using the standard technique. The whole treatment planning procedure, in the same sequence, was checked independently by a second neurosurgeon.

Results

Figure 1 shows a transverse slice in which CT and 3D angiographic data are displayed in a checkerboard pattern, allowing easy recognition of alignment. The same is available in any arbitrary plane orientation. Figure 2 depicts a 3D reconstruction based on CT scanning- and angiography-derived data concerning a right-sided, medium-sized pericallosal AVM. The colored surface represents the 70% isodose surface from a five-arc radiosurgical treatment plan. Figure 3 demonstrates three orthogonal views of a 3D-reconstructed angiogram of a right-sided, small, insular AVM fed by lateral lenticulostriate arteries. The colored surface represents the 70% isodose surface from a five-arc radiosurgical treatment plan.

The follow-up period ranged from 1 to 6 months. Up-to-date (June 2002) clinical data were available for all 20 patients. None of the patients experienced complications from the radiosurgical procedure, and to date we have not observed any hemorrhage in treated patients. The follow-up period is too short to allow evaluation of the success rate based on complete obliteration of the nidus AVM; however, this was not the aim of the present study. A comparison of the two treatment planning modalities demonstrated that the new procedure allows safe and accurate radiosurgical treatment. In other words, using the new method of 3D angiography our study confirmed the same choices of isocenter numbers and collimator diameters in all patients. In five patients the 3D procedure suggested minor changes in target coordinates, but these corrections never exceeded 1 mm (range 0.3–1 mm, mean 0.7 mm).

Table 1 shows the relative number of patients harboring AVMs in whom the target coordinates were changed after the 3D study, as they were distributed into three classes of target volume (< 1 cm³, 1–4 cm³, and > 4 cm³). Table 2 offers a description of the relevant clinical and dosimetric characteristics in this group, together with the relative amount and direction of the shift in coordinates.
Limitations of Biplanar Angiography for Radiosurgery

For many years, angiography has represented the first choice in the examination leading to the diagnosis of cerebral AVMs and, until the introduction of CT and MR imaging, angiography was the only available imaging database for AVM radiosurgery.10,23 Given the availability of computer-based TPSs, the reliance on biplanar stereotactic angiography alone is now considered inadequate. The basic problem is that angiograms are two-dimensional projections of three-dimensional lesions. These images lack the third dimension and this shortcoming has been recognized as a possible source of inaccuracy in nidus definition.7,13,17,18,20,22,24 For this reason, the inclusion of true 3D images in the treatment planning process has been advocated as a means for increasing the accuracy and decreasing the side effects of stereotactic radiosurgery. Blatt, et al.,7 have demonstrated in a series of 81 patients that the differences between nidus definition observed on angiograms and CT scans were of major clinical importance. In 44 patients who were treated (54%), the inclusion of CT data resulted in a mean isocenter shift of 3.6 mm. In an equal number of patients, the diameter of the collimator was changed (increased in 14 cases and decreased in 30). In 20 patients with large (> 10 cm³) AVMs Levy, et al.,19 added CT and MR imaging to angiography in a multimodality-based treatment session. The iterative delineation of target volume resulted in significant modifications from the initial target volumes defined using angiography. Substantial amounts of apparently normal tissue were excluded from the final target, and additional abnormal vascular structures were identified in all patients. Today the radiosurgical gold standard requires the combination of stereotactic angiography and stereotactic CT and/or MR imaging.13,17–19

Usefulness of 3D Imaging of Intracranial Vessels

Although stereotactic, high-resolution, contrast-enhanced CT scanning improves target volume definition, it is unable to discriminate between the AVM's arteriolar nidus, which must be obliterated, and normal vessels such as feeding arteries or draining veins, which should be spared. These features are clearly identifiable on an angiographic study that consists of a series of images obtained at different times after injection of contrast material. An improvement in radiosurgical treatment planning demands an examination that is both angiographic and truly 3D. Consequently, 3D angiography has been suggested to increase the accuracy of treatment planning for AVM radiosurgery.16

Aoki, et al.,4 relied on CT angiography for dose planning in a series of 76 patients who underwent radiosurgery for AVMs. Dynamic CT scanning with intravenous injection of contrast material and 3D vessel reconstruction improved delineation of the AVM nidi and draining vessels. A significant reduction in target volume was reported. The ability of CT angiography to discriminate arteries feeding the AVM within the vessel architecture, however, was considered inferior to that of stereotactic angiography. Moreover, spatial accuracy perpendicular to the slice plane is expected to be dependent on slice thickness and, in general, is poorer than that lying on the axial plane.

Kondziolka, et al.,17 selected stereotactic MR angiography to target AVMs in 28 patients and compared treatment planning based on this imaging modality with that obtained using stereotactic angiography. In all cases plans based on stereotactic MR angiography were completed first and then superimposed on angiograms for a comparison. In 16 patients (57%) stereotactic MR angiography provided critical information on the shape of the AVM that was not provided by conventional angiography. In three patients plans based on stereotactic MR angiography were clearly superior be-
cause stereotactic angiography alone could have led to an overestimation of the size of the nidus. In one case, however, angiography revealed a small separate AVM nidus that was missed by stereotactic MR angiography.

In 22 patients Bednarz, et al.,9 combined stereotactic angiography and 3D time-of-flight MR angiography in treatment planning: in 12 patients (55%) the treatment plans were modified after inclusion of the MR angiography data.

As suggested by Friedman,12 these studies proved only that 3D stereotactic imaging is essential for treating the entire AVM nidus and sparing surrounding normal tissue. The authors did not compare the quality of 3D information provided by MR angiography with that obtained using contrast-enhanced CT scanning and, consequently, the evidence that plans based on stereotactic MR angiography are in any way superior to those obtained using a combination of stereotactic angiography and stereotactic contrast-enhanced CT scanning (today’s gold standard) is still lacking.

Recently Kakizawa, et al.,16 emphasized the importance of 3D rotational angiography in the evaluation of the structure of an AVM. They have concluded that the information obtained would improve strategies of treating large and complex AVMs, enabling compartmental embolization, safe staged resection, and reduction of the AVM size for radiosurgery. Nevertheless, they did not provide any method for locating 3D angiography in stereotactic space.

Foreseeing its possible use in stereotactic procedures, Bridcut, et al.,6 evaluated the accuracy of 3D reconstruction in a 3D rotational angiography system. They found a maximum error of 1.4 mm in target location and concluded that this level of accuracy enables use of spatial data for intervention. Again, they did not provide methods for using these data in stereotactic space.

**Image Fusion Procedure**

We rely on an image fusion procedure to locate 3D angiography in stereotactic space.

Image fusion is a method that combines complementary information from two separate imaging modalities into a single imaging study.15,25 In its most frequent application, the image fusion procedure is based on surface matching between corresponding volumes identified using both methods of imaging. In radiosurgical practice, image fusion has been used mainly for correcting magnetic field distortion and for using MR imaging data for treatment planning. Image fusion between nonstereotactic MR images and stereotactic CT scans has been reported to be accurate and reliable by Alexander, et al.,2 in a series of 28 consecutive cases of radiosurgical treatment planning. According to these authors, the technique of intermodality image fusion among MR imaging, CT, single-photon emission CT, and positron emission tomography studies, combined with the ability to fuse images obtained at different times along the course of an illness, provides additional advantages for the precise evaluation of treatment effects and complications. In the meantime, this procedure has gained wide acceptance in radiosurgical practice.9,18,20 Most image fusion techniques are completely automatic procedures, based on surface matching or on the maximization of mutual information.2,14,25 Our procedure of 3D angiography–stereotactic CT image fusion is still an iterative manual procedure. Despite the fact that image fusion is dependent on the operator’s experience and ability, it proved reliable and precise in this study. Of course, automatic techniques were considered. None of them has been used thus far in our clinical practice, because of difficulties we found that were related to data characteristics. In fact, vessel intensities are similar to those of bone and, moreover, the volume reconstructed by 3D angiography is restricted, precluding the use of external localizers or “error bars.” For the same reason, characteristic structures of the skull are often cut off (see, for example, Fig. 1, in which portions of the frontal bone and eyeballs are missing in the angiographic reconstruction). To overcome these restrictions, we are studying an automatic matching method that optimizes similar measures based on the overlapping voxel intensities from each data set. The process is fully automatic, resulting in the proper alignment of both imaging studies, which are brought into the same spatial matrix. This procedure has been tested on data sets associated with three patients in the present series who have already been treated and preliminary results seem to be satisfactory.

**Three-Dimensional Rotational Angiography for Radiosurgical Treatment Planning and Follow-Up Review**

We have shown that nonstereotactic 3D angiography, undertaken without a head frame and localizers, can be located in stereotactic space by applying an image fusion procedure that adds stereotactic CT scanning. Treatment planning based on the data provided seems to be equivalent to that based on data from up-to-date standard methods of using stereotactic angiograms in combination with CT scans. In our preliminary experience, the main features of treatment planning were not influenced by implementation of 3D angiography in 15 of 20 patients; this is explained, at least in part, by the fact that the two different angiograms were placed in the same study of reference, the stereotactic CT scan. A second possible reason for the coincidence in target identification could be that the standard and 3D procedures were performed during the same planning ses-

**Table 2**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Location of AVM</th>
<th>Target Volume (cm³)</th>
<th>No. of Isocenters</th>
<th>Coordinate Shift (mm)</th>
<th>Direction of Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42, F</td>
<td>cerebellar</td>
<td>0.2</td>
<td>1</td>
<td>1.0</td>
<td>lat</td>
</tr>
<tr>
<td>6</td>
<td>30, F</td>
<td>deep occipital</td>
<td>1.7</td>
<td>1</td>
<td>0.7</td>
<td>vert</td>
</tr>
<tr>
<td>10</td>
<td>29, M</td>
<td>brainstem</td>
<td>0.3</td>
<td>1</td>
<td>0.5</td>
<td>pst/lat</td>
</tr>
<tr>
<td>17</td>
<td>19, M</td>
<td>deep temporal</td>
<td>0.5</td>
<td>1</td>
<td>0.3</td>
<td>pst/med</td>
</tr>
<tr>
<td>18</td>
<td>33, F</td>
<td>parietal</td>
<td>3.7</td>
<td>2</td>
<td>1.0</td>
<td>vert</td>
</tr>
</tbody>
</table>

*Med = medial; pst = posterior; vert = vertical.*
— one immediately after the other— by the same radiosurgical team. We recognize that this fact may obscure the importance of the 3D technique for improving the target definition; the alternative would have been to have two independent radiosurgical teams, each one blinded to the plan designed by the other, working on the standard and 3D methods, respectively, and then compare the results. In radiosurgical treatment planning, however, target delineation is still the personal decision of the neurosurgeon on the case; in this setting, it would be impossible to measure whether any significant variance should be found between the results of independent teams and the relative importance of different techniques and different operators.

Regarding the five patients in whom the 3D study suggested coordinate modification, the number is too small to allow any strong and significant conclusion. The relative preponderance of AVMs with small volumes needs to be confirmed by a subsequent series. If confirmed, this fact would suggest that 3D angiography, with its possibility to display reconstructions from multiple viewpoints, could be particularly useful for target identification in cases of small AVMs that are partially hidden by nearby vessels on standard stereotactic projections.

In our opinion, the main advantage of the new procedure consists of the possibility of relying on a frameless, nonstereotactic angiography study for target definition in stereotactic space. In AVM radiosurgery, 3D rotational angiography could be performed at a different site and during a different time with respect to the irradiation procedure. Moreover, 3D angiography studies performed for follow up at different times after irradiation can be fused with the stereotactic CT scans used for treatment planning for accurate evaluation of the evolution of the nidus obliteration process. Relying on existing broadband Internet connections, a complete 3D angiography examination could be transmitted in approximately 15 minutes. This could be used to create a network in which many institutions offering neuroradiology could be related to a single radiosurgical unit, with the aim of actively contributing to radiosurgical treatment planning and follow up.

Moreover, the image fusion procedure can also be used to combine 3D rotational angiography with nonstereotactic CT examinations performed without a head frame or localizer, also in extracranial locations. With this capability, the procedure could also be used for accurate treatment planning of radiosurgical procedures that are performed using frameless, image-guided, computer-assisted robotic apparatuses.

Conclusions
To our knowledge, this is the first time a method for performing AVM radiosurgical treatment planning based on frameless, nonstereotactic, 3D rotational angiography has been reported. Three-dimensional angiography was fused with stereotactic contrast-enhanced CT scanning. The treatment plan that was obtained has been compared with that acquired using the standard procedure of imaging and has proved reliable and accurate in a series of 20 patients. The procedure allows an improved spatial representation of the target with respect to biplanar stereotactic angiography. Because 3D rotational angiography does not require head fixation, greater freedom in the time and location of treatment planning is allowed. Using the same image fusion procedure, follow-up 3D angiograms can be fused to the images used in the treatment planning process and utilized for a precise evaluation of the outcome of AVM radiosurgery.

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Three-dimensional angiography for radiosurgery


Manuscript received July 1, 2002.
Accepted in final form November 19, 2002.

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