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### Superselective Angio-CT of Brain Tumors

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**PURPOSE:** To determine the efficacy of superselective angio-CT in the diagnosis of astrocytoma. **METHODS:** Nineteen patients with astrocytomas had superselective angio-CT before chemotherapeutic agents were administered via superselective intraarterial infusion. CT was performed after contrast material was delivered through a microcatheter, which had been advanced into the feeding arteries of the tumor. Superselective angio-CT scans were compared with digital subtraction angiograms, conventional contrast-enhanced CT scans, and contrast-enhanced T1-weighted MR images. **RESULTS:** Superselective angio-CT scans depicted contrast enhancement of the tumor in all of the patients and the medullary veins of the tumors in 32% of the patients. Digital subtraction angiograms showed tumor stains in 68% of the patients and the medullary veins in only 5%. Conventional CT scans and MR images showed contrast enhancement of the tumor in 89% of the patients. Superselective angio-CT scans confirmed the proper position of the catheter tip for the infusion of a chemotherapeutic agent. **CONCLUSIONS:** Superselective angio-CT can be used to depict contrast enhancement of tumors and the vascular structures that are characteristic of astrocytomas.

Index terms: Astrocytoma; Brain neoplasms, computed tomography; Computed tomography, technique

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Arterial angio-computed tomography (angio-CT), performed with contrast administration directly into arteries through a catheter, has been used in the diagnosis of various lesions in the liver (1–3), lung (2), and other organs (4– 6). As previously reported, arterial angio-CT can depict vascular structures of tumors, which, because arteries and veins in the lesions can be seen with better contrast resolution, is useful in the differential diagnosis (1, 6). The advent of microcatheters (7) has made possible the use of superselective catheterization for such intravascular procedures as embolization of arteriovenous malformations and aneurysms, and thrombolytic therapy.

AJNR 17:1073-1080, June 1996 0195-6108/96/1706-1073 © American Society of Neuroradiology For the treatment of brain tumors, direct intraarterial infusion of chemotherapeutic agents is known to have pharmacokinetic advantages (8–11). In our institution, patients with gliomas have been treated with a combination of radiation and superselective intraarterial infusion of chemotherapeutic agents. To confirm the distribution of these drugs, we performed arterial angio-CT with superselective administration of contrast material, a procedure that we have named *superselective angio-CT*.

Superselective angio-CT scans showed the distribution of contrast material as well as new findings concerning the vascular structure of the brain tumors. The purpose of this study was to compare superselective angio-CT scans with digital subtraction angiograms, conventional enhanced CT scans, and magnetic resonance (MR) images to determine the efficacy of superselective angio-CT in the depiction of tumors.

#### **Subjects and Methods**

Between March 1993 and November 1994, superselective angio-CT was performed in 19 patients with astrocy-

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Fig 1. Injection protocol for superselective angio-CT.

tomas who expected to be treated with superselective intraarterial infusion of 1-(4-amino-2-methyl pyrimidine-5yl)-methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride (ACNU) (12). Informed consent was obtained from the patients and/or their families before the examinations.

All tumors were proved histologically by biopsy or surgery. Four astrocytomas were grade II, 10 were grade III, and 5 were grade IV. Superselective angio-CT was performed before superselective infusion of ACNU. The patients underwent transfemoral catheterization with a 6F catheter (PU; Toray, Tokyo, Japan). The catheter was placed in either the cervical internal carotid artery or the cervical segment of a vertebral artery. After intraarterial digital subtraction angiography with the PU catheter, a Tracker-18 catheter (Target Therapeutics, Los Angeles, Calif) was passed coaxially inside the PU catheter and advanced into the feeding arteries of the tumor. Heparinized saline was administered through the PU and Tracker-18 catheters. Once the Tracker catheter was in the proper position, digital subtraction angiography was performed with a hand injection of diluted contrast material. Patients were then moved to the CT suite.

Axial CT of the whole brain was first performed parallel to the orbitomeatal plane without contrast administration. A section including tumor was scanned before contrast injection, and then four contiguous scans at the same section were obtained with contrast injection into the feeding arteries. The scanning protocol is illustrated in Figure 1. A 9800 CT scanner was used, with 2-second scanning time, 170 mAs, and 10-mm collimation. These 10-mmthick sections were chosen to gain an improved signal-tonoise ratio.

For superselective angio-CT, it is necessary to dilute the contrast material before superselective intraarterial injection, owing to the possibility of blood-brain barrier disruption; therefore, 0.5 mL of iopamidol diluted with 2.5 mL of saline was administered by hand injection at a rate of 1 mL/s. When necessary, subtraction images with an edge enhancement were obtained by using the Data View System (GE Medical Systems, Milwaukee, Wis). If superselective angio-CT did not show proper positioning of the infusion catheter, the catheter tip was withdrawn proximally and the imaging procedure was repeated. After completion of the CT studies, the patient was returned to the angiography suite, where the position of the tip of the catheter was confirmed. ACNU was administered in a dose of 50 to 80 mg, dissolved in sterile water in a concentration of 2.5 mg/mL, with use of a mechanical injector at a rate of 80 mL/h.

The tip of the Tracker catheter was in the horizontal portion of the middle cerebral artery in 4 patients, in the insular portion of the middle cerebral artery in 12, in the opercular portion of the middle cerebral artery in 1, in the horizontal portion of the anterior cerebral artery in 1, in the superior cerebellar artery in 1, and in the posterior cerebral artery in 1.

All patients had conventional enhanced CT and contrast-enhanced T1-weighted MR imaging within 2 weeks before the superselective angio-CT study. Conventional enhanced CT was performed parallel to the orbitomeatal plane with 2-second scanning time, 170 mAs, and 10-mm collimation. Enhanced T1-weighted MR images were acquired on a 1.5-T unit. Four-millimeter-thick sections with a 2-mm section gap were obtained parallel to the plane including the anterior and posterior commissures, using a spin-echo sequence (400–600/20–40/2 [repetition time/ echo time/excitations]).

To evaluate tumor stain (contrast enhancement) and the presence of medullary veins (13, 14) in the tumor, we retrospectively compared superselective angio-CT scans with conventional digital subtraction angiograms obtained via infusion through the guiding catheter, superselective digital subtraction angiograms obtained via infusion through the Tracker-18 catheter, conventional enhanced CT scans, and contrast-enhanced T1-weighted MR images. Scans were examined conjointly by more than three observers, including a neuroradiologist. Evaluation of the appearance of tumor stain, the contrast enhancement of the tumor, and the medullary veins was by consensus.

#### Results

Superselective angio-CT scans depicted contrast enhancement of tumor in all patients (100%) and the medullary veins (Figs 2 and 3) in 6 (32%) of 19 patients (Table). In comparison, conventional or superselective digital subtraction angiograms depicted tumor stain in 13 (68%) of 19 patients and the medullary veins in 1 (5%); and conventional enhanced CT scans or contrast-enhanced T1-weighted MR images showed contrast enhancement of tumor in 17 patients (89%) (Table). All 4 grade II tumors (cases 8, 10, 11, and 15), which enhanced on routine imaging, were histologically proved by biopsy alone, so they may have been of higher grade. Superselective angio-CT scans depicted contrast enhancement of tumor in 2 patients in whom no contrast enhancement was seen on the conventional enhanced CT scans and MR images (Fig 4). Contrast enhancement was seen in normal and abnormal tissue during the early phase of superselective angio-CT. During the late phase, however, superselective anAJNR: 17, June 1996





Fig 2. Case 3: 51-year-old man with residual grade IV astrocytoma after surgery.

Conventional contrast-enhanced CT scan (*A*) shows tumor in left frontal lobe (*arrows*); superselective angio-CT scan with contrast administration into the insular portion of the left middle cerebral artery (*B*) shows enlarged medullary veins (*arrowheads*) in the tumor.



Fig 3. Case 8: 38-year-old man with grade II astrocytoma.

Contrast-enhanced T1-weighted MR image (*A*) shows tumor in right frontal and temporal lobe (*arrowheads*); superselective angio-CT scan (*B*) with contrast administration into the insular portion of the right middle cerebral artery shows enlarged abnormal vessels (*arrows*) in the tumor, which are presumably medullary veins draining into the subependymal vein (*arrowheads*) of the lateral ventricle.

gio-CT showed contrast enhancement only of tumor tissue (Fig 4). In 6 patients, superselective angio-CT clearly showed irregular tumor vessels draining into the enlarged medullary veins and the subependymal veins of the lateral ventricle (Figs 2 and 3). The enlarged medullary veins did not appear in normal tissue. Those veins seemed to appear early; however, it was not evident because we could not differentiate between the arterial and the venous phases.

In a patient with astrocytoma in the parahippocampal gyrus (case 10, Fig 5), superselective angio-CT with contrast injection into the posterior cerebral artery ensured proper positioning of the catheter tip for the infusion of ACNU. Superselective angio-CT was also useful in identifying a feeding artery in another patient (case 5) with astrocytoma in the left frontal lobe. In no patient did the catheter tip retract or move during transfer to the CT scanner or upon return to the angiography suite. No significant complication resulted from catheterization or contrast administration.

#### Discussion

Arterial angio-CT is known to be a useful diagnostic tool for tumors of the liver (1–3), because it affords excellent contrast resolution for differentiating normal from abnormal attenuation areas. Angio-CT can be performed either with an intravenous bolus infusion of contrast material or via direct intraarterial administration through a catheter. The former is a well-known

Com	parison	of sı	perselective	angio-CT	with	other	imaging	technig	ues

Case	Age, y/ Sex	Grade of Astro- cytoma	Radiation dose, Gy	Location of Tumor	Location of Tip of Microcatheter	Tumor Stain	Contrast Enhancement of Tumor			Medullary Veins		Comments
						DSA	СТ	MR	Angio-CT	DSA	Angio-CT	
1	69/M	Ш*	28	L frontal	L M2	+	+	+	+	-	-	
2	50/M	Ш	60	L frontal, parietal	L M2	+	+	+	+	-	—	
3	51/M	IV	60	L frontal	L M2	+	+	+	+	_	+	Fig 2
4	52/M	Ш	60	Cerebellum	R SCA	-	-	-	+	-	_	Fig 4
5	30/M	IV	60	L frontal	L A1, M1	+	+	+	+	-	-	†
6	41/F	Ш*		L frontal	L M2	+	+	+	+	-	-	
7	52/F	Ш*		R frontal, parietal	R M2	+	+	+	+	-	_	
8	38/M	П*	60	R frontal, temporal	R M2	+	+	+	+	-	+	Fig 3
9	57/M	Ш	•••	L frontal, parietal	L M2	+	+	+	+	-	-	
10	46/M	Ш*		R temporal, parietal	R PCA	_	+	+	+	-	-	Fig 5†
11	43/F	<b>II</b> *		L frontal	L M3	-	+	+	+	_	-	
12	49/M	Ш	60	R basal ganglia	R M2	_	-	-	+	-	—	
13	65/M	IV		R frontal	R M2	+	+	+	+	+	+	
14	38/M	Ш	60	R frontal	R M1	-	+	+	+	_	+	
15	19/M	<b>II</b> *	28	L frontal	L M2	+	+	+	+	—	-	
16	26/F	Ш		R frontal	R M1	+	+	+	+	—	-	
17	41/M	Ш		R temporal	R M1	+	+	+	+	-	_	
18	51/F	IV	60	L frontal	L M2	-	+	+	+	-	+	
19	64/M	IV	24	R frontal	R M2	+	+	+	+	-	+	

Note.—+ indicates detectable; –, not detectable; DSA, digital subtraction angiography; M1, horizontal portion of the middle cerebral artery; M2, insular portion of the middle cerebral artery; M3, opercular portion of the middle cerebral artery; A1, horizontal portion of the anterior cerebral artery; PCA, posterior cerebral artery; and SCA, superior cerebellar artery.

\* Histology was proved at biopsy.

† Angio-CT was useful for determining the proper position of the catheter tip for the infusion of a chemotherapeutic agent.

noninvasive technique for detecting vascular lesions, such as aneurysms (15–17). Arterial angio-CT has been widely used in detecting liver metastasis (3). Angio-CT with contrast administration into the superior mesenteric artery can show a small tumor in the liver not discernible by conventional enhanced CT. Angio-CT has also been used to identify the feeding artery of liver tumors before embolization (2).

Encouraging results of intraarterial infusion of chemotherapeutic agents have been reported (8–11). It has been shown, for example, that intraarterial infusion of carmustine (BCNU) to the brain resulted in a considerably higher drug level in the infused areas than that attained with intravenous delivery. Intraarterial delivery of carmustine to brain tumors might also be achieved in higher concentrations. However, to avoid toxic reactions to the eye as a complication of internal carotid arterial infusion of chemotherapeutic agents, the catheter should be introduced into the supraclinoid or a more distal segment (18, 19).

With the advent of microcatheters, superselective catheterization has become an easy and safe procedure (7). In our institution, patients with glioma have been treated with a combination of radiation and superselective intraarterial infusion of ACNU (12). Initially, we attempted superselective angio-CT to confirm the distribution of contrast material through the catheter tip before infusion of ACNU. We found that superselective angio-CT scans showed contrast enhancement of the tumor even in cases in which no such enhancement was seen on conventional CT scans or contrast-enhanced T1-weighted MR images. However, this finding might be the result of increased contrast resolution caused by administration of contrast material directly into the feeding arteries.



Fig 4. Case 4: 52-year-old man with grade III astrocytoma in the cerebellar vermis.

Conventional contrast-enhanced CT scan (A) 1 week after surgery shows brain loss caused by removal of tumor (*arrows*); however, residual tumor anterior to the site of prior tumor resection (confirmed surgically) is not seen. Superselective digital subtraction angiogram (B) 3 weeks after surgery shows catheter tip (*arrow*) in the right superior cerebellar artery, but tumor stain is not depicted. An early phase of superselective angio-CT (C) with contrast administration into right superior cerebellar artery shows contrast enhancement of right cerebellar hemisphere and the vermis. The late phase (D) and its subtracted image (E) show residual tumor stain (*arrowheads*) anterior to the brain loss.

Enlarged medullary veins are usually found in two pathologic processes: malignant infiltrating gliomas and arteriovenous malformations (20). They may also be seen in other lesions of the white matter, such as metastasis, malignant lymphoma, cerebral hemorrhage, inflammatory diseases, and venous thrombosis (20). Huang and Wolf (21) reported that in approximately 10% of their patients with glioblastoma multiforme, no vascular abnormalities appeared other than enlargement of the deep medullary veins, and they concluded that streaming within the deep medullary veins was a reliable sign of glioblastoma multiforme. Hooshmand et al (22) noted that the deep medullary veins were seen in low-grade astrocytomas where there was central necrosis. In a case of astrocytoma grade II in our series, the enlarged medullary veins were seen on superselective angio-CT scans. These veins appeared early, as they were draining arteriovenous shunting in the tumor. Scatliff et al (23) studied the vascular structure of glioblastomas on postmortem specimens and reported four major types of vascular components: type I, cortical and transcortical (medullary) arteries draining into the enlarged medullary veins and subependymal veins; type II, gray matter hypervascularity consisting of Fig 5. Case 10: 46-year-old man with grade II astrocytoma.

Contrast-enhanced T1-weighted MR image (A) shows tumors in right temporal (arrows) and parietal lobes. Superselective digital subtraction angiogram (B) in the right posterior cerebral artery shows catheter tip (arrow) but does not clearly show tumor stain. An early phase of superselective angio-CT (C) with contrast administration into right posterior cerebral artery shows contrast enhancement of normal tissue, but it does not depict tumor stain. A superselective angio-CT scan (D) obtained after the catheter tip (arrow) was pulled slightly proximally shows contrast enhancement corresponding to the tumor (arrowheads).



neocapillary circulation and vasodilatation of cortical arteries and veins; type 3, irregular neocapillary formation around necrotic areas; and type 4, a rounded capillary network around necrotic area or in viable tumor. In our series, cases 3 (Fig 2), 8 (Fig 3), 13, and 14 seem to fit the type I category, and this was clearly seen on the superselective angio-CT scans. These enlarged medullary veins were seen on digital subtraction angiograms that had an increased spatial resolution. Until now, this radiologic finding could be seen only on conventional or digital subtraction angiograms. Superselective angio-CT made it possible to depict this angiographic finding by CT.

Superselective angio-CT scans seem similar to microangiographic sections obtained by postmortem injections. In investigations of the vascular structure of tumors, this new technique is superior to digital subtraction angiography, conventional enhanced CT, and contrast-enhanced T1-weighted MR imaging. The type of vascular structure reported by Scatliff et al (23) is thought to be characteristic of glioma.

Superselective angio-CT has also proved useful in identifying feeding arteries that were unclear on conventional or digital subtraction angiograms. In 2 patients (cases 5 and 10) in our series, only superselective angio-CT scans showed the major feeding artery of the tumor. This indicated that superselective angio-CT is valuable at the time of intraarterial infusion of chemotherapeutic agents and will be feasible for evaluation of feeding arteries before chemotherapy. Moreover, this technique is useful for determining the proper position of a catheter tip prior to infusion of chemotherapeutic agents (Fig 5). The distribution of contrast material seen on the superselective angio-CT scan, however, may not be representative of the depiction of ACNU distribution, because the infusion rate of contrast material is quite different from that of ACNU; moreover, contrast material has a higher specific gravity than drugs. To assess the exact distribution of intraarterial cerebral chemotherapeutic agents, single-photon emission CT (SPECT) performed with intraarterial administration of technetium-99m hexamethylpropyleneamine oxime (HMPAO) has recently been proposed (24). Aoki et al (24) studied drug distribution with <sup>99m</sup>Tc HMPAO SPECT and reported that uniform distribution could be obtained by manual pulsatile injection (24, 25).

The technique presented here, while attractive for the depiction of the character and vascularity of tumors, can be safely performed with modern digital subtraction angiographic equipment, mounted on a C-arm, and with high-resolution fluoroscopy and road-mapping capabilities. Moving patients to a CT suite is necessary for superselective angio-CT; therefore, new equipment combining angiography and CT is expected. We encountered no complications resulting from catheterization and injection of contrast materials. Although this study is preliminary, our findings suggest that implementation of superselective angio-CT might facilitate improved survival rates for patients with brain tumors. Our results should encourage further evaluation of the effectiveness and safety of superselective angio-CT.

In conclusion, we performed superselective angio-CT in patients with astrocytomas immediately before superselective intraarterial chemotherapy. Superselective angio-CT scans depicted contrast enhancement of the tumors in all patients and made it possible to see the enlarged medullary veins that are characteristic of gliomas. This technique can be used to identify feeding arteries that are unclear on angiograms as well as to determine the proper position of a catheter tip before injection of chemotherapeutic agents.

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