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AJNR Am J Neuroradiol 1998, 19 (4) 641-647

<http://www.ajnr.org/content/19/4/641>

This information is current as
of August 29, 2025.

Diagnosis of Brain Death Using Two-Phase Spiral CT

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PURPOSE: The purpose of this study was to determine the utility of spiral CT in the diagnosis of brain death.

METHODS: Spiral CT was evaluated prospectively in 14 brain-dead patients and in 11 healthy subjects. A two-phase protocol was used. Twenty seconds after intravenous injection of a nonionic iodinated contrast medium, the CT table was drawn through the gantry at a rate of 10 mm/s while scanning was in progress. The second scanning phase was started automatically a mean of 54 seconds later, using the same parameters. Opacification or absence of opacification of carotid, vertebral, and basilar arteries and intracerebral veins was ascertained for each image in both phases. The diagnosis of brain death was confirmed by electroencephalography (n = 7), angiography (n = 5), or both (n = 2). Statistical analysis with the Fisher exact test enabled us to compare the brain-dead patients with the healthy control subjects.

RESULTS: In brain death, the pericallosal and terminal arteries of the cortex did not opacify during the two phases of spiral CT, whereas the superficial temporal arteries were always visible. The internal cerebral veins, the great cerebral vein, and the straight sinus did not opacify, whereas the superior ophthalmic veins were visible on both sides 13 times. For each vessel type, specificity was 100% for nonvascular opacification criteria on the right and left sides.

CONCLUSION: Two-phase spiral CT can demonstrate the absence of intracerebral blood flow in brain death.

The diagnosis of brain death must respect all the guarantees required by law and be determined as early as possible to avoid unnecessary treatment and to allow organ harvesting for transplantation (1–3). Clinical criteria for brain death include deep unresponsive coma, no brain stem function (no pupillary light or corneal, oculocephalic, oculovestibular, oropharyngeal, or tracheal reflexes) and no spontaneous ventilation (4). Although these criteria alone are sufficient to establish brain death in some countries (5), additional investigative procedures are required in others. Two neurophysiological methods are used to demonstrate the cessation of brain function: elec-

troencephalography (EEG) (6, 7) and brain stem auditory evoked potentials (8). The EEG, despite its limitations, is more reliable, as it can show electrocerebral silence.

Among the techniques measuring cerebral blood flow, conventional angiography of the four cerebral arterial axes is the reference standard for imaging brain death (9–17). Spiral computed tomography (CT) (18–20) offers a new means of evaluating vascular anatomy after intravenous injection of a timed bolus of contrast material. It is relatively noninvasive and represents an interesting alternative to conventional angiography for physiological evaluation of blood flow in brain arteries and veins.

The purpose of this study was to determine the accuracy of two-phase spiral CT, as compared with conventional angiography and EEG, in demonstrating the absence of intracerebral circulation in brain death.

Methods

Spiral CT was evaluated prospectively over a 12-month period in 14 patients diagnosed as brain dead and in 11 control subjects.

Received July 9, 1997; accepted after revision October 17.

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Patients (Table 1)

All patients admitted to the Medical Intensive Care Unit and the Trauma Intensive Care Unit with head injury, intracranial hemorrhage, cerebral ischemia, and clinical suspicion of brain death were considered eligible for the study. Patients met the inclusion criteria when brain death was either confirmed by two isoelectric EEGs or by an absence of cerebral blood flow at cerebral angiography. Nine patients had EEG and spiral CT,

and seven patients had cerebral angiography and spiral CT. Two patients had both EEG and cerebral angiography. All patients were mechanically ventilated with a P_{CO_2} of 35 to 40 mm Hg, and arterial oxygen tension (P_{O_2}) was above 70 mm Hg. When necessary, arterial blood pressure was sustained at above 100 mm Hg by dopamine infusion during CT and arteriography.

TABLE 1: History and investigative procedures for all patients (n = 14) with brain death

Patient	Age, y/Sex	Pathology	Conventional Angiography (n = 7)	EEG (n = 9)
1	51/F	HI + SAH	...	ECS
2	25/M	HI + SAH	...	ECS
3	47/F	CD	...	ECS
4	20/F	HI + SAH	...	ECS
5	47/M	HI + SAH	+	ECS
6	49/M	HI + SAH	...	ECS
7	15/M	HI + SAH	+	...
8	55/M	HIT + SAH	+	...
9	34/F	ICH + SAH	+	...
10	30/F	HI + SAH	+	...
11	9/M	HI	...	ECS
12	24/M	HI	+	...
13	19/M	HI + SAH	+	ECS
14	46/F	PFI	...	ECS

Note.—HI indicates head injury; ICH, intracranial hemorrhage; SAH, subarachnoid hemorrhage; CD, carotid dissection; PFI, posterior fossa ischemic infarction; +, typical findings of brain death present; and ECS, electrocerebral silence.

TABLE 2: Spiral CT findings in the first phase

Arteries/Veins	Postinjection Mean Time, s	No. of Opacified Vessels				Fisher's Exact Test*	Specificity, %†
		Normal CT (n = 11)		Brain Death (n = 14)			
		R	L	R	L		
C-ICA	20	11	11	5	5	S	100
C-ECA	20	11	11	14	14
C-VA	20	11	11	5	4	S	100
BA	24	...	11	...	0	S	100
STA	25	11	11	14	14
IC-ICA	26	11	11	4	3	S	100
SC-ICA	27	11	11	2	1	S	100
M1-MCA	27	11	11	2	1	S	100
P1-PCA	27	11	11	0	0	S	100
A1-ACA	27	11	11	1	0	S	100
PCA	28	11	11	0	0	S	100
TAC	28	11	11	0	0	S	100
IJV	22	0	0	0	0
SOV	27	1	1	9	0
ICV	28	11	11	0	0	S	100
SSS	28	...	11	...	0	S	100
GCV	28	...	11	...	0	S	100
SS	28	...	11	...	0	S	100

* Test significant if $P < .05$.

† Specificity criteria: arteries or veins not visible in cases of brain death.

Note.—C-ICA indicates internal carotid artery (cervical level); C-ECA, external carotid artery (cervical level); C-VA, vertebral artery (cervical level); BA, basilar artery; STA, superficial temporal artery (frontal and parietal branches); IC-ICA, intracavernous internal carotid artery; SC-ICA, supracavernous internal carotid artery; M1-MCA, middle cerebral artery (M1 segment); P1-PCA, posterior cerebral artery (P1 segment); A1-ACA, anterior cerebral artery (A1 segment); PCA, pericallosal artery; TAC, terminal arteries for the cortex; IJV, internal jugular vein (foramen level); SOV, superior ophthalmic vein; ICV, internal cerebral vein; SSS, superior sagittal sinus; GCV, great cerebral vein; and SS, straight sinus.

EEG

Two EEG recordings within an interval of 6 hours were obtained in nine of 14 patients. An eight-channel apparatus (Alvar-France) was used, with a sensitivity of $2 \mu V/min$, a constant time of 0.3 seconds, no filter, and an electrode impedance of less than 10 kilohms. Electrodes were positioned according to the 10–20 international system. Bipolar assemblies with large interelectrode distances were used. The EEG was recorded for 30 minutes and during several painful stimulations.

Spiral CT

Fourteen patients were imaged as soon as possible after the first EEG. A topogram of the cervical spine and head was obtained for locating the skull base and the second cervical vertebral body. The gantry was not angled, but the patient's head was positioned parallel to the orbitomeatal line, and the starting point was selected at the C1–2 cervical level.

Initially, 10-mm unenhanced images were obtained through the entire brain at 10-mm intervals. Twenty seconds after injection of nonionic contrast medium (120 mL iohexol) into an antecubital vein at a rate of 3 mL/s using a power injector and an 18-gauge catheter, the CT table was drawn through the gantry at a rate of 10 mm/s while scanning was in progress (250 mA, 120 kV, 1-second scan time, 320×320 matrix, 14-second continuous exposure, 10-mm collimation, pitch of 1). The sec-

TABLE 3: Spiral CT findings in the second phase

Arteries/ Veins	Postinjection Mean time, s	No. of Opacified Vessels			
		Normal CT (n = 11)		Brain Death (n = 14)	
		R	L	R	L
C-ICA	54	11	11	11	13
C-ECA	54	11	11	14	14
C-VA	54	11	11	14	14
BA	58	...	11	...	2
STA	59	11	11	14	14
IC-ICA	59	11	11	8	8
SC-ICA	60	11	11	6	5
M1-MCA	60	11	...	6	5
P1-PCA	60	11	11	3	3
A1-ACA	60	11	11	4	4
PCA	61	11	11	0	0
TAC	61	11	11	0	0
IJV	56	11	11	8	11
SOV	60	3	3	13	13
ICV	61	11	11	0	0
SSS	61	...	11	...	7
GCV	61	...	11	...	0
SS	61	...	11	...	0

Note.—C-ICA indicates internal carotid artery (cervical level); C-ECA, external carotid artery (cervical level); C-VA, vertebral artery (cervical level); BA, basilar artery; STA, superficial temporal artery (frontal and parietal branches); IC-ICA, intracavernous internal carotid artery; SC-ICA, supracavernous internal carotid artery; M1-MCA, middle cerebral artery (M1 segment); P1-PCA, posterior cerebral artery (P1 segment); A1-ACA, anterior cerebral artery (A1 segment); PCA, pericallosal artery; TAC, terminal arteries for the cortex; IJV, internal jugular vein (foramen level); SOV, superior ophthalmic vein; ICV, internal cerebral vein; SSS, superior sagittal sinus; GCV, great cerebral vein; and SS, straight sinus.

ond scanning phase was started automatically (a mean of 54 seconds later) from the same C1–2 cervical level after preprogramming for the same parameters as those used for the first phase. As each spiral acquisition took 14 seconds, the second helical scan began 54 to 60 seconds after initial injection of contrast medium. Axial images (10-mm sections) were then reconstructed with 5-mm increments. Scanning allowed for visualization of vessels from the C1–2 cervical level to the convexity, providing a total coverage of 14 cm. During this entire procedure, systolic blood pressure was maintained above 100 mm Hg.

Eleven adults (six men and five women; mean age, 48 years, range, 19 to 66 years) with no cerebral lesions were used as control subjects after informed consent was obtained. All were studied with the same spiral CT protocol.

Conventional Cerebral Angiography

Immediately after spiral CT scanning, arterial digital subtraction angiography (ADSA) was carried out in seven patients to demonstrate intracerebral circulatory arrest. Arteriography was performed by the Seldinger femoral approach using a 5F catheter and selective injection into the two common carotid arteries and the two vertebral arteries. Six to 10 mL of nonionic contrast medium (iohexol) was injected into the common carotid artery and 4 to 6 mL into the vertebral artery. The flow rate was 4 mL/s, with two images per second during the first 5 seconds, followed by one image every 2 seconds during the next 25 seconds (ie, with a delay until 55 seconds after the start of the injection).

Spiral CT studies were interpreted by two radiologists who were aware that each patient had clinical brain death but unaware of the results of conventional angiography.

Results

In all nine brain-dead patients, both EEG examinations showed electrocerebral silence. For each of the 14 brain-dead patients and 11 control subjects, selected vessels (veins and arteries) were analyzed on each of the 5-mm reconstructed sections at the different time points after intravenous administration of contrast medium. The time points at which these evaluations occurred corresponded to the mean times obtained in the control subjects for each vessel opacified (Tables 2 and 3).

The first phase (Table 2) corresponded to the initial arterial opacification beginning 20 seconds after injection. Comparisons between control subjects and brain-dead patients were made according to the Fisher exact test and based on the presence or absence of opacification of each vessel visualized. For each vessel type (Table 2), specificity was 100% for nonvascular opacification criteria for the right and left sides. External carotid arteries (mean time, 20 seconds) and superficial temporal arteries (mean time, 25 seconds) were opacified in all cases, indicating that contrast medium had been injected correctly. The internal jugular veins (foramen level) were never visualized, since the axial view was obtained before venous blood return (mean time, 22 seconds).

For the 11 control subjects, all arteries were opacified in the first phase (Fig 1). For brain-dead patients, basilar arteries, posterior cerebral arteries (P1 segment), pericallosal arteries, and terminal arteries for the cortex never opacified (Fig 2). The middle cerebral artery (M1 segment) was weakly opacified in two brain-dead patients (on both sides in one, on the right side only in the other). The anterior cerebral artery (A1 segment) was weakly visualized in a single brain-dead patient (right side only). The internal carotid arteries were opacified at the cervical level (n = 5), intracavernously (n = 4) or supracavernously (n = 2), and the vertebral arteries were opacified in five brain-dead subjects.

In control subjects (mean time, 28 seconds), the internal cerebral veins, the superior sagittal sinus, the great cerebral vein, and the straight sinus were always opacified, whereas the superior ophthalmic veins were opacified in only one patient (barely visible because of their small 1-mm diameter). In brain-dead patients, the internal cerebral vein, the superior sagittal sinus, the great cerebral vein, and the straight sinus were never opacified, whereas the superior ophthalmic veins (diameter, 3 to 4 mm) were clearly visualized in nine patients. One patient had a facial injury with orbital lesions (fracture and hematoma), which made it difficult to evaluate the superior ophthalmic veins.

In the second phase (Table 3), all vessels (arteries and veins) were opacified in control subjects except

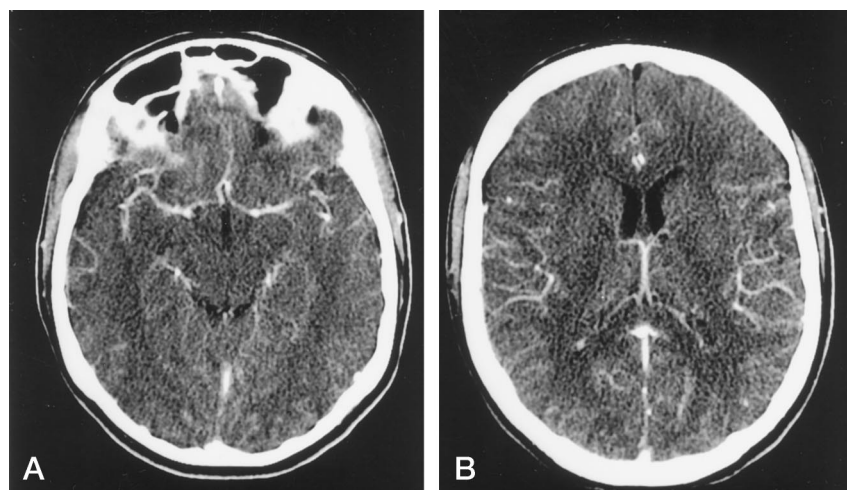


FIG 1. Spiral CT: first phase in a healthy adult.

A, Twenty-six seconds after intravenous injection of nonionic contrast medium, all arteries are opacified: anterior cerebral arteries, middle cerebral arteries, posterior cerebral arteries, and superficial temporal arteries.

B, Two seconds later and a section above A: on the midline of the brain, the pericallosal arteries, internal cerebral veins, great cerebral vein, straight sinus, and superior sagittal sinus are opacified. Terminal arteries for the cortex are also well opacified.

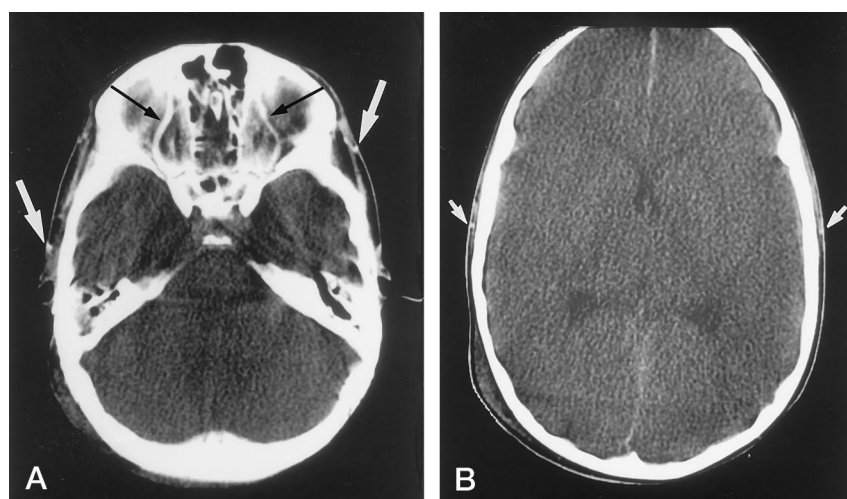


FIG 2. Brain death.

A, The first phase of spiral CT 25 seconds after intravenous injection of contrast medium: the cerebral arteries and the basilar artery are not visible, whereas the superficial temporal arteries (white arrows) and superior ophthalmic veins (black arrows) are opacified.

B, Three seconds later, neither midline vessels (arteries and veins) nor terminal arteries for the cortex are seen, whereas superficial artery branches (arrows) are opacified. Note brain swelling.

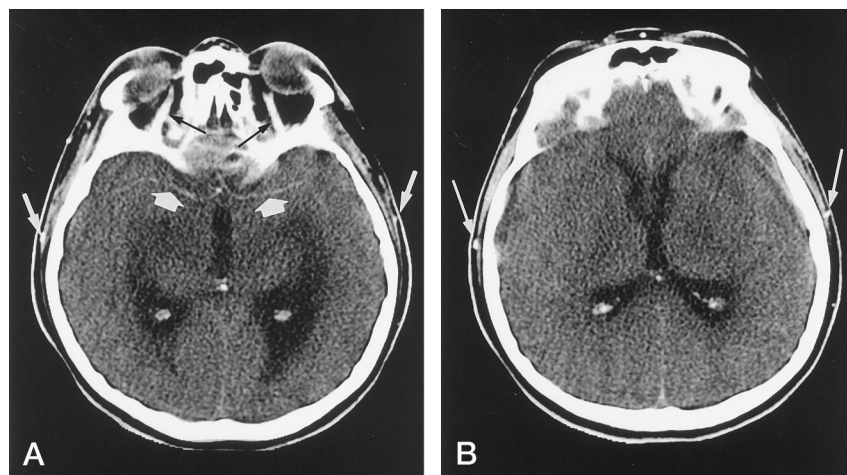


FIG 3. Brain death on axial CT sections obtained from bottom to top.

A, Diagnosis of brain death in the second phase of spiral CT 60 seconds after injection: the middle cerebral arteries (M1 segment) and anterior cerebral arteries (A1 segment) are thin and elongated, with narrow arrest of opacification (short white arrows) corresponding to "stasis filling." The distal branches of the external carotid arteries (superficial temporal arteries) are still opacified (long white arrows). They were already visible during the first phase, as the external carotid network is normally opacified during brain death. The superior ophthalmic veins (black arrows) are well opacified.

B, Corresponding section, obtained 1 second later shows lack of opacification of intracerebral arteries and veins, indicating the arrest of intracranial circulation, whereas the external carotid network (arrows) is opacified.

for the superior ophthalmic veins (diameter, 1 to 2 mm), which were visible in only three subjects. In the 14 brain-dead patients, the pericallosal artery and the terminal cortical arteries were never opacified, whereas the superficial temporal arteries were always visible. Delayed opacification was noted in proximal segments M1 (n = 6), A1 (n = 4), and P1 (n = 3) and in the basilar artery (n = 2). In all these cases, the M1,

A1, and P1 segments were thin and opacified over a short distance, thus differing from the normal pattern. Internal jugular venous blood return (jugular foramen) was seen eight times on the right side and 11 times on the left, and the superior sagittal sinus was opacified seven times. The internal cerebral vein, great cerebral vein, and straight sinus were never opacified, whereas the superior ophthalmic veins

were seen on both sides 13 times, appearing dense and wide (diameter, 3 to 4 mm) (Fig 3).

In the seven brain-dead patients who were studied, ADSA demonstrated intracerebral circulatory arrest, decreased circulation in the internal carotid and vertebral arteries associated with stagnation and arrest of contrast medium at various levels (Table 4), and no evidence of venous drainage by the great cerebral vein and straight sinus 55 seconds after injection. The superior ophthalmic veins were always opacified and clearly visible (Fig 4). The branches of the external carotid arteries were opacified and washed out quickly, whereas contrast medium remained in the internal carotid and vertebral arteries.

In the seven brain-dead patients, the superior ophthalmic veins were opacified at both spiral CT and ADSA. In three patients, the levels of contrast me-

dium arrest in the internal carotid and vertebral arteries were the same with both techniques. Arrest levels were underestimated by ADSA in four patients as compared with spiral CT: at the basilar artery level ($n = 1$) and the C4 level ($n = 3$). In one patient, the M1 segment was not visible by ADSA and was thin and only faintly seen on spiral CT scans (Table 5).

In the seven patients who did not undergo ADSA, spiral CT showed arrested intracerebral circulation, and EEG confirmed an absence of cerebral function.

Discussion

Conventional arteriography is currently considered to be the most valid method for demonstrating brain

TABLE 5: Two-phase spiral CT arrest level and superior ophthalmic vein visibility in comparison with angiographic findings in seven patients

Patient	Two-Phase Spiral CT Arrest Level					
	Internal Carotid Artery		Vertebral Artery		Superior Ophthalmic Vein	
	R	L	R	L	R	L
5	C	C	FM	FM	+	+
7	C	C	BA*		+	+
8	C4	C4	C	C	+	+
9	A1-M1	C4*	BA		+	+
10	C4*	C4*	C	C	+	+
12	M1*	M1*	FM	C	+	+
13	C	C	C	C	+	+

* Arrest level underestimated by carotid arteriography.

Note.—C indicates cervical level; C4, intracavernous level; C5, intrapetrous level; A1-M1, subarachnoid arterial segments; BA, basilar artery; +, superior ophthalmic veins opacified; FM, foramen magnum.

TABLE 4: Angiographic findings in seven patients

Patient	Conventional Angiographic Arrest Level					
	Internal Carotid Artery		Vertebral Artery		Superior Ophthalmic Vein	
	R	L	R	L	R	L
5	C	C	FM	FM	+	+
7	C	C	C	FM	+	+
8	C4	C4	C	C	+	+
9	A1-M1	C5	BA	C	+	+
10	C5	C5	C	C	+	+
12	C5	C	FM	C	+	+
13	C	C	C	C	+	+

Note.—C indicates cervical level; C4, intracavernous level; C5, intrapetrous level; A1-M1, subarachnoid arterial segments; BA, basilar artery; +, superior ophthalmic veins opacified; and FM, foramen magnum.

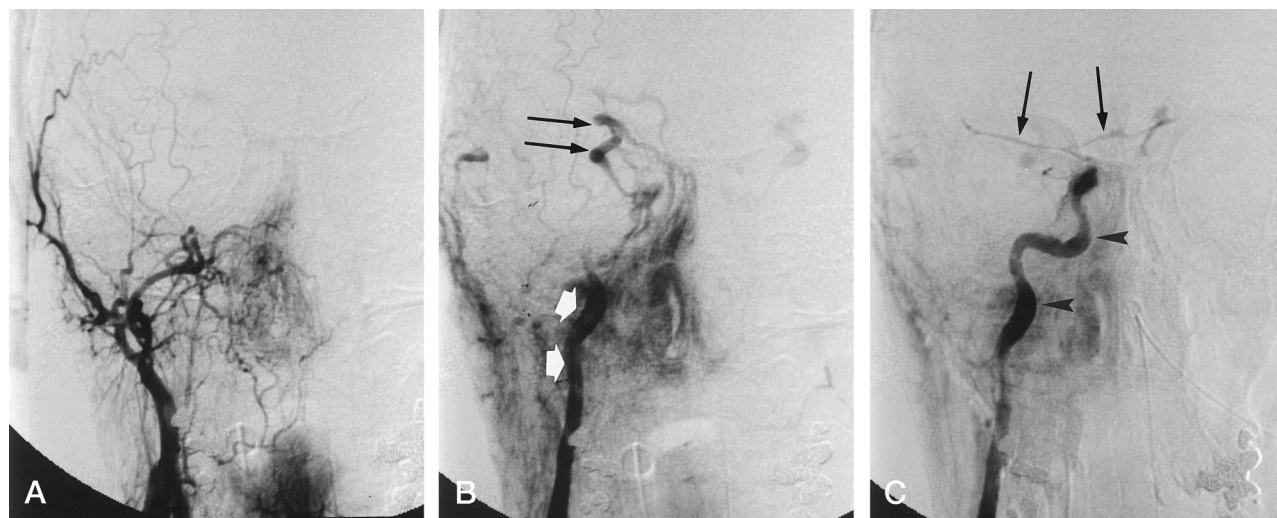


FIG 4. Arterial digital subtraction angiography for the right common carotid artery in brain death.

A, Three seconds after injection in the common carotid, the external carotid artery and its branches are clearly visualized, whereas the internal carotid artery is not yet opacified. Note opacification of the nasal mucosa.

B, Seven seconds later, the right superior ophthalmic vein is well opacified (black arrows), while opacification of the internal carotid artery (white arrows) occurs late and slowly (the intracavernous segment is not yet visible).

C, Twenty-five seconds after intraarterial injection, intracerebral arrest is demonstrated, with stagnation of contrast medium in the internal carotid artery (arrowheads). Note the thin, elongated features of the A1 and M1 segments, corresponding to "stasis filling" (arrows).

death (21–23). If two-phase spiral CT is to replace conventional arteriography for this purpose, it must be capable of satisfying all criteria indicative of absence of intracerebral blood flow. Our results indicate that two-phase spiral CT could replace four-vessel conventional arteriography in the diagnosis of brain death. According to French law, the diagnosis of brain death is based on complete and persistent absence of consciousness, spontaneous breathing, and all brain stem reflexes, as well as on the results of two isoelectric EEGs, usually performed within a 6-hour interval. When an EEG cannot be performed or is uninterpretable because of hypothermia, metabolic disorders, or drug intoxication, cerebral angiography can be used to demonstrate the cessation of cerebral blood flow.

Spiral CT shows the stagnation and arrest of contrast medium at the level of the internal carotid and vertebral arteries, associated with the absence of venous blood return. Enhanced visibility of the superior ophthalmic veins attests to the asynchronism of venous blood return and confirms the diagnosis, in combination with absence of opacification (with 100% specificity) of the pericallosal artery, terminal arteries for the cortex, internal cerebral vein, great cerebral vein, and straight sinus. With two-phase spiral CT, this absence of arterial and venous opacification is due to cessation of brain blood flow, even though systolic blood pressure in our patients was maintained above 100 mm Hg.

Our protocol required scanning of the brain before contrast medium was injected to ascertain the presence of such abnormalities as edema, ischemic infarction, and intracranial hemorrhage. Subarachnoid hemorrhage (24) would not decrease visibility of the median-line vessels (pericallosal artery, internal cerebral vein, or great cerebral vein).

Spiral CT allows for evaluation of vascular anatomy and rapid visualization of a large number of vessels after intravenous administration of a timed bolus of contrast medium (20, 25). The arterial phase can be studied before the venous system is enhanced. The bolus is then gradually diluted by the central blood pool. Arterial anatomy well beyond the A1 and M1 segments of the anterior and middle cerebral arteries can easily be visualized with this technique (25), as can the terminal arteries for the cortex if sufficient contrast medium (120 to 150 mL) is used. The adequate mean interval for visualization of the carotid arteries is 20 seconds after the start of injection (18). Normal cerebral circulation was observed at that time and 8 seconds later as venous blood in control subjects (26), but was never observed in brain-dead patients. The second phase (mean, 61 seconds after the beginning of injection) confirmed the cessation of brain flow, since no arterial or venous opacification was evident. In brain death, cessation of brain blood flow occurs when the intracranial pressure is higher than the systemic arterial pressure (10). During the second phase of spiral CT in our study, delayed opacification and stagnation of contrast medium were noted in basal arachnoid arterial segments, which

were thin. This condition, which was also apparent at conventional angiography, has been referred to as subarachnoid “stasis filling” (27). Similar angiographic findings have been reported in 10 of 65 clinically brain-dead patients (28).

The superior sagittal sinus was seen in the second phase of spiral CT in 50% of the brain-dead patients in our study. This has also been described by Lee et al (29), in the absence of arterial cerebral perfusion, in 26 of 53 brain-dead patients investigated by ^{99m}Tc -HMPAO scintigraphy. Visualization of the superior sagittal sinus probably results from external carotid artery perfusion through meningeal vessels or from emissary veins and does not contradict the diagnosis of brain death (14, 29). The enhanced bilateral superior ophthalmic veins that we observed in 13 of 14 brain-dead patients seemed to be an indirect sign apparently not described before. In one patient, these veins could not be seen because of severe facial-orbital injury. This sign may be due to the presence of vascular anastomoses at the level of the orbits between the external carotid arteries (facial artery, superficial temporal artery, infraorbital artery) and the ophthalmic artery. These anastomoses could become functional through inversion of circulation toward the ophthalmic artery in patients with thrombosis of the internal carotid artery (30). Moreover, occlusion of the internal carotid artery is a cause of increased external carotid flow that may account for the “hot nose sign” described in a nuclear medicine study on the diagnosis of brain death (31) and in an MR imaging study (17) in which a hot spot represented collateral and extracranial circulation through the center of the face. Moreover, elevated intracranial pressure and/or possible cavernous sinus thrombosis during brain death could hinder usual drainage through the cavernous sinus, in which case the superior ophthalmic veins could drain through the facial and infratemporal venous system. Blood flow in the ophthalmic artery could also account for the retinal activity detected on the EEG in patients with brain death and in patients with low cerebral blood output. In our study, spiral CT imaging of the superior ophthalmic veins was always confirmed by conventional angiography, which, however, underestimated the level of arterial circulatory arrest in the four patients. This may have been due to the larger dose of contrast medium injected during spiral CT and its better resolution of thin structures.

Our results suggest that findings for two-phase spiral CT correlate closely with brain death criteria demonstrated by conventional angiography (21). Vascular opacification by conventional angiography or two-phase spiral CT is now obtained with nonionic products that are well tolerated at concentrations below 5 mL/kg (32).

Although there is agreement about the clinical requirements for a diagnosis of brain death, opinions differ concerning the complementary techniques. Because the EEG recordings may be difficult to interpret (6, 7, 33), transcranial Doppler sonography can be performed to confirm cerebral circulatory arrest

(13, 28, 34–37). However, this examination is operator-dependent, so that brain stem auditory evoked potentials are not reliable (38, 39). Scintigraphic methods (14, 15, 40, 41) are efficient but costly, and diagnosis of brain death by nuclear MR imaging (42), although reliable, is difficult to obtain in ventilated patients.

Conclusion

Cessation of cerebral flow can be demonstrated by conventional angiography, which allows diagnosis of brain death. However, this procedure is expensive and time consuming and requires a relatively large and well-trained staff (11). Our current protocol with two-phase spiral CT can be applied easily and with no errors, as compared with conventional angiography and EEG. Two-phase spiral CT can demonstrate the absence of intracerebral blood flow in brain death.

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