Brain Death Diagnosis: A Radiologist matter when patient cannot undergo a physical exam

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Learning objectives

Study the situations when clinical criteria of Brain Death cannot be applied and further ancillary tests are required

Remember the available electrophysiological tests (EEG, EMG) and the situations in which they are usually "used"

Illustrate the role of the different imaging procedures, included CTA and CTP in diagnosis of Brain Death, keeping in mind their limitations in certain clinic situations
Background

Brain Death is the permanent and irreversible cessation of brain functions. It manifests as lack of response to stimuli, absence of muscular activity and a flat electroencephalogram for a specific length of time.

TOOLS FOR DIAGNOSIS OF BRAIN DEATH:

The diagnosis of Brain Death can usually be made clinically, but in when clinical criteria cannot be applied, we need ancillary tests to confirm it.

Clinical Criteria:

Absence of all brain functions as proven by neurologic examination, with all of the following findings:

• Coma

• Absent brain-originating motor response, including response to pain stimulus above the neck

• Absent pupillary light reflex; pupils are midposition or dilated (4 to 9 mm)

• Absent corneal reflexes

• Absent oculo-vestibular reflexes (caloric responses)

• Absent jaw jerk

• Absent gag reflex

• Absent cough with tracheal suctioning

• Absent sucking or rooting reflexes

• Apnea as demonstrated by apnea test (not demonstrable in CO2 retainers and may be aborted due to apparition of arrhythmias and hypotension

*In the presence of medical confounders, clinical criteria cannot be applied
• **Complicating medical conditions**: Severe electrolyte, acid-base, endocrine, or circulatory disturbance (shock)

• **No drug intoxication** or poisoning

• **Core temperature >36ºC** or hypothermia

• **Low blood pressure** <100 mg Hg (vasopressors may be required)

*Observation Period:*

In children, it's mandatory between 12 and 48 hours, depending on their age: 48 hours for children under 2 months, 24 hours for children between 2 months and 1 year, and 12 hours for those under 18 years.

In adults it's optional (compulsory depending on legislation of different countries):

6 hours generally recommended, up to 24 hours in hypoxic-ischemic encephalopathy or resuscitation after cardiac arrest, and up to 3 days in cases of induced hypothermia.

[1 Wijdicks: The Diagnosis of Brain Death. NEJM 2001]

**Ancillary Tests:**

They must be used when clinical criteria cannot be applied, and are also necessary to assess brain death in children under 1 year of age (in children under 2 months of age, 2 positive tests are needed). They can also be used to shorten the observation period.

a) Electroencephalogram (EEG): Positive if electrocerebral silence or flat EEG during a 30-minute recording at increased sensitivity, but:

- doesn't reveal potentials from **subcortical structures** (brainstem, thalamus)

- may not reveal potentials in some cases of **sedation, hypothermia** and **metabolic factors** (conditions usually found in the Intensive Care Units)

- In these cases Evoked Potentials have better results (combined with EEG), but blood flow tests are more accurate.

b) Imaging of brain blood flow:
Radiologists demonstrate the complete cessation of blood flow to the brain. Brain Death is associated to a rise in intracranial pressure (as in oedema Fig. 6 on page 6 or mass effect Fig. 7 on page 6 Fig. 8 on page 7). When intracranial pressure exceeds systemic arterial pressure, there is no blood flow to the brain Fig. 9 on page 8.

We may prove this by demonstrating lack of opacification of arteries and veins or lack of brain perfusion. Fig. 10 on page 9.

These exams provide less false positives in cases of **sedation, hypothermia and metabolic factors**. On the other hand they can give some false negatives in situations that lower intracranial pressure (trauma, surgery, ventricular drain and open sutures Fig. 15 on page 14) and systemic arterial pressure must be over **100 mmHg** for the result to be reliable.

- **Angiography:** is the classic gold standard. It’s invasive and not widely available.

- **SPECT:** Detects brain perfusion of isotope 99Tc-HMPAO, between 30 minutes and 2 hours after its injection. Limited by lack of isotopes in some hospitals and technicians not available 24 hours.

- **Eco-Doppler:** Gives more false positives than the other tests.

- **CTA:** Is accurate, available 24 hours, quick and easy to perform. It evaluates other structures and may show the cause of the death (hematomas Fig. 12 on page 11 or extensive infarcts Fig. 13 on page 12).

- **CTP:** Reveals real lack of perfusion Fig. 11 on page 10, even in cases of **hypotension**, but only evaluates a limited anatomic territory. When intracranial vessels are not visible, perfusion maps can be achieved by a non deconvolution analysis technique Fig. 14 on page 13 or by using the superficial temporal artery as the reference.
Fig. 6

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Fig. 7

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Fig. 8

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Fig. 9

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**Fig. 10**

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Fig. 12

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Fig. 14

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Fig. 15

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Imaging findings OR Procedure details

CTA Protocol:

1) Non enhanced CT: may show brain swelling Fig. 16 on page 21, haemorrhage Fig. 17 on page 22, cerebral herniation Fig. 18 on page 23, diffuse hypodensity (with associated pseudo-subarachnoid haemorrhage Fig. 19 on page 24), etc

2) CTA: Injection of 2 ml/kg of contrast at 2.5 ml/s and 2 series at arterial (20s) and venous times (60s). Blood pressure must be over 100 mmHg.

3) CTP: More sensitive, can be performed when a false negative is suspected.

It's a quick and low invasive exam to show the absence of brain flow or brain perfusion. Rise of contrast-induced nefropathy is not demonstrated. [2 Lima FO, AJNR 2009 Dec 31]

There are 2 different protocols of evaluation of brain vessels:

a) 7 vessels protocol: Lack of enhancement of the 2 medial cerebral arteries (M4), the 2 anterior cerebral arteries (A3) Fig. 1 on page 17, the 2 internal cerebral veins and the great cerebral vein Fig. 3 on page 18 Fig. 4 on page 19

b) 4 vessels protocol: Lack of enhancement of the 2 medial cerebral arteries at M4 Fig. 5 on page 20 and the 2 internal cerebral veins Fig. 20 on page 25 Fig. 21 on page 26 Fig. 22 on page 27 Fig. 23 on page 28. An study of 105 patients demonstrated that this protocol has 100% of specificity for diagnosis [3 Frampas. CT Angiography of Brain Death Diagnosis. AJNR 2009]

Score is 0 to 4, giving 1 point per non-opacified artery.

The lack of enhancement of the internal cerebral veins is the most sensitive finding.
**Fig. 1:** Enhancement of Anterior Cerebral Artery in A3 (pericallosal artery)

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**Fig. 2:** Faint enhancement of Anterior Cerebral Artery A3 in a false negative of Brain Death due to craniectomy

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Fig. 3: Filling of Medial Cerebral Artery in M4 (cortical arteries) as well as both Internal Cerebral Veins and the Great Cerebral Vein.

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Fig. 4: More subtle filling of Internal Cerebral Arteries and the Great Cerebral Vein. False negative in a 71 year old male who suffered a right posterior cerebral artery infarct, with an avascular brainstem.

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Fig. 5: Narrowing of both medial cerebral arteries with persistent filling of some of the cortical branches (M4), so brain death could not be assessed in this 60 year-old woman who suffered a cerebellar hematoma.

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Fig. 16

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Fig. 17

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Fig. 18: Subfalcine herniation in a 74 year old man, with great expansivity due to a left medial cerebral artery infarct

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Fig. 19: 54 year old man who committed suicide with ansiolytics. The diffuse hypodensity of the cerebral parenchyma in the unenhanced CT makes vessels seem more dense, giving the fake appearance of a subarachnoid haemorrhage.

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**Fig. 20:** 49-year old male with a hypoxic ischemic encephalopathy. Patent opacification of the internal carotid arteries, without enhancement of any of the intracerebral vessels.

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**Fig. 21:** Stroke of right medial crebral artery, worsening despite intravenous fibrinolysis. The CTA shows no enhancement of medial cerebral arteries

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Fig. 22: No visibility of medial cerebral artery in a 59 year old man injured after a fall from his vehicle.

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Fig. 23: 16-months-old boy who suffered a traffic accident. Faint opacification of medial cerebral arteries, not further than M1. There was no visible cortical artery (M4)

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Conclusion

- Brain death is the complete and irreversible loss of brain function

- Diagnosis of brain death is usually made by neurologic examination

- Ancillary tests are required when clinical criteria cannot be applied and to supplement the clinical examination in children < 1 year

- Tests of brain blood flow may be preferred to electrophysiological tests in the setting of hypothermia and metabolic or drug confounders

- CTA can provide a quick and widely available blood flow diagnostic test to improve brain death diagnosis support

- The 4-vessels protocol has proven to be an accurate analysis of CTA
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