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# Decompressive craniectomy may cause diagnostic challenges to assess brain death by computed tomography angiography

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## Abstract

**Background:** According to Italian legislation to diagnose brain death (BD) after the initial documentation of the clinical signs, repetition of clinical testing and confirmation of the loss of bioelectrical activity of the brain (EEG) is required. However, when EEG is unreliable it is necessary to demonstrate cerebral circulatory arrest (CCA). Accepted imaging techniques to demonstrate CCA include: cerebral angiography, cerebral scintigraphy, transcranial Doppler (TCD) and computed tomography angiography (CTA). This latter technique, due to its large availability, low invasivity and easy and fast acquisition is widely used over the country. Nevertheless its diagnostic reliability is affected by some limitations in patients with decompressive craniectomy.

**Methods and Results:** Here we report two cases of brain injury with clinical signs of BD and at the same time, opacification of intracranial arteries on CTA and a pattern consistent with flow arrest on the corresponding insonable arteries on TCD.

**Conclusion:** The discrepancy between CTA and TCD results points out a methodology limitation that could be overcome by updating Italian legislation according to other European Countries legislation.

**Key words:** Brain death, Computed Tomography Angiography, Transcranial Doppler Sonography

## Introduction

A factor limiting organ donation in Italy is the availability of suitable brain-death (BD) organ donors. Italian legislation defines the diagnostic procedures for determining BD (Law no. 578 dated 29/12/1993 and Ministerial Decree no. 582 dated 22-Aug-1994 recently updated by Ministerial Decree dated 11/04/2008): after initial documentation of the clinical signs of BD, repetition of clinical testing and confirmation of the loss of bioelectrical activity of the brain is required. However, some cases need demonstration of cerebral circulatory arrest (CCA) such as children under one year and clinical situations which do not allow a definite aetiopathogenetic diagnosis or are likely to interfere with the overall clinical-instrumental findings, including the presence of CNS depressants, facial or head trauma or recent surgery which may prevent recording of brain electrical activity or testing of brain stem reflexes.

According to Italian legislation each hospital can choose the method to confirm CCA depending on technical instrumentation and personnel skills available. The National Advisory Committee on Organ Transplantation (NACOT) recently drafted guidelines for the application of instrumental cerebral blood flow (CBF) evaluation, updated to 20/02/2009. Accepted imaging techniques for the measurement of CBF include: cerebral angiography, cerebral scintigraphy, transcranial Doppler (TCD) and CT angiography (CTA).<sup>1-6</sup> This latter technique, due to its large availability, low invasivity and easy and fast acquisition is widely used over the country.<sup>5-6</sup> Nevertheless its diagnostic reliability is affected by some limitations. Here we report two cases of brain injury with clinical signs of BD and at the same time, opacification of intracranial arteries on CTA and a pattern consistent with flow arrest on the corresponding insonable arteries on TCD.

## Case 1.

A 38 year old patient was admitted to our emergency department after a motorcycle accident. On arrival he was on cardiac arrest. An advanced cardiac life support was immediately performed until return of spontaneous circulation (ROSC) after 10 minutes of chest compressions. On stabilization of vital signs, the GCS was 3. An urgent CT scan detected a large subdural haematoma within the left hemisphere causing midline shift and compression over homolateral ventricular system. In association there were basilar skull and cervical vertebrae fractures. A consultant neurosurgeon decided for an emergency decompressive craniectomy and evacuation of the subdural haematoma. Thereafter he was transferred to our ICU for specific monitoring and management. On admission he was unconscious, without reaction to painful stimuli. Pupils were 1mm and did not respond to light. Corneal reflexes were absent. Spontaneous respiration was insufficient so artificial ventilation was continued. He was treated according to the local protocol for the treatment of acute brain injury aiming at maintaining adequate cerebral perfusion. The CBF was monitored daily with TCD (Multi-Dop® Digital, Compumedics DWL, Germany). On day five the clinical examination fulfilled the criteria for BD but

according to the consultant neurophysiologist a complete electrode coverage for EEG was not accessible due to the recent craniectomy.

The TCD conducted using both temporal acoustic windows revealed intracranial bilateral blood flow through the middle cerebral artery (MCA) and the anterior cerebral artery (ACA), with left prevalence. Since insonation of the subtentorial arteries was difficult for the risk of dislocation of cervical fractures, a TCA was asked. This exam was carried out by a 64-slice volumetric CT Scanner (GE Fairfield, CT - USA) and demonstrated CBF through the main intracranial arteries despite a threadlike opacification of the basilar artery (BA). *Fig. 1a.*

The day after a new TCD showed bidirectional flow at both MCAs level, systolic spikes at the left ACA level, impossibility to insonate the right ACA. According to the NACOT guidelines, these criteria suggest flow arrest. Nevertheless an evaluation of distal vertebral arteries and BA is needed. A new CTA showed internal carotid artery (ICA) and MCA opacification on the side of craniectomy. On the opposite side the absence of filling from the petrous portion of the ICA was shown. *Fig. 1b.*

## Case 2.

A 36 year old man was admitted after a car accident. On arrival the patient was unconscious, unable to react to any stimulus, his pupils were non reactive. He was spontaneously breathing, SpO<sub>2</sub> was 98% on oxygen but his blood gas analysis revealed acidosis. After intubation and hemodynamic stabilization a CT scan showed a left occipital skull fracture with an epidural left temporal haemorrhage associated with intraparenchymal petechial haemorrhage.

The patient underwent an emergency fronto-temporo-parietal craniectomy and evacuation of the haematoma. Intraoperative findings showed a linear skull fracture extending across a venous sinus causing extensive bleeding.

He was transferred to our ICU without any change in neurological assessment. He maintained mechanical ventilation but spontaneous breathing was present. He was treated according to the same local protocol applied before and CBF was monitored daily with TCD. After 7 days he developed the clinical criteria for BD. As before, the EEG was technically unfeasible due to the recent surgery. The TCD showed bilateral bidirectional flow reversing on MCAs and systolic spikes at the posterior cerebral arteries level.

Again, the insonation of subtentorial arteries was hazardous for the presence of cervical fractures. The CTA showed bilateral opacification of the petrous portion of ICAs. (*Fig 2*)

In both patients cardiac death occurred few days after. During this period, they never fulfilled the CTA criteria to diagnose CCA.

## Results

The ancillary tests here described were performed according to Italian legislation and NACOT guidelines. Nevertheless their results were discrepant. Namely, bidirectional flow in TCD was confirmatory of flow arrest on insurable arteries whereas the CTA revealed opacification of corresponding intracranial arteries. We could not diagnose BD in these two potential organ donors.

## Discussion

BD in Italy is defined as “the irreversible loss of all the functions of the brain”. CBF measurements are necessary in some particular cases defined in Law no. 578 dated 29/12/1993.<sup>1</sup> The D.M. 582/94 and to the NACOT guidelines define very strictly methods and times for the correct execution of CTA leading to more accurate standardization and leaving less space to subjectivity in the interpretation of the exam. Nevertheless, when intracranial pressure is lowered by craniectomy, opacification of intracranial arteries on CTA may occur despite circulation is affected.

With its rate of 21.9 organ donors PMP, Italy is the third country within the European Union regarding organ donation, after Spain (29.2) and France (22.8).<sup>7</sup> However the rate of organ donation can increase: according to the Italian National Institute of Statistics, deaths from road accidents in 2010 in Italy have been 4,090. The mean age of deaths for males was 20-24 years, but high rates of deaths were also registered within 25 to 29 and 30 to 34.<sup>8</sup> Some considerations may derive from these numbers: first, the population considered is quite young, being then ideal potential organ donors. Second, in our experience, patients involved in road accidents are more likely to present to the emergency department with cerebral mass lesions needing emergency surgery. Emergency evacuation of a mass lesion is generally combined with decompressive craniectomy to favour brain perfusion. Despite the craniectomy by itself is not a factor affecting the reliability of EEG, a large recent craniectomy, mostly if brain swelling is present, can interfere with minimum technical standards to perform EEG causing its unreliability or unfeasibility. This is one of the cases contemplated by Italian law, in which the evaluation of cerebral blood flow is mandatory. As CTA is emerging as the alternative to conventional angiography, its diagnostic limitations in patients with decompressive craniectomy may be an important limiting factor for organ procurement in our country.

The main factor limiting organ donation in Italy is the lack of family consent, whereas preconceived attitudes about this issue can interfere with the final decision and socio-economic and socio-demographic variables (patient's age, cause of death, race) and religious belief play a significant role. Educational efforts should be increased to overcome these limitations, however the results may require a long period of time to be measurable. An upgrade of the current interpretative guidelines for BD diagnosis can give faster results, although less significant.

We are not the first to report that decompressive craniectomy may affect the diagnosis of BD with CTA. Berenguer *et al.* noted that decompressed patients with a clinical BD and absence of brain perfusion demonstrated with nuclear medicine perfusion test, showed minimal flow on CTA.<sup>9</sup> Dupas *et al.* in 1998 defined the criteria for BD diagnosis with spiral CT. They noted that in BD the pericallosal and terminal arteries of the cortex, the internal cerebral veins, the great cerebral vein and the straight sinus did not opacify on spiral CT.<sup>10</sup> Since then, several studies permitted French legislation to define the actual criteria for BD confirmation by CTA based on the lack of opacification of 7 intracerebral vessels. On these basis Frampas *et al.* constructed a 4-point CTA score based on the lack of opacification of 4 cerebral vessels on the CT scan acquired starting 60 seconds after the contrast medium injection commenced.<sup>11</sup> In the specific case of decompressive craniectomy, the French Society of Neuroradiology recommends that, if arterial opacification occurs, the deep venous network should be evaluated and BD can be confirmed in the absence of opacification of the left and right internal cerebral veins and of the great cerebral vein. In Spain, CTA is accepted as confirmatory test for diagnosing brain death. Again, the study of the venous flow is required, although Spanish guidelines do not enter in the specific case of decompressive craniotomy.<sup>12,13</sup>

We did not perform the evaluation of venous drainage as acquisition starting 20 seconds after the contrast medium injection is recommended by Italian guidelines for the diagnosis of CCA by CTA. Nevertheless, the only evaluation of artery phase can be misleading, showing “opacification” which may not mean “circulation”. In our cases, the cerebral arteries that opacified on CTA, evaluated by TCD showed a pattern consistent with absence of flow. On the contrary, there are reports of false-negative results in cases of skull defects using TCD to detect CCA in brain death with flat EEG<sup>14</sup>. In addition, the need for confirmatory testing has been questioned by some authors who claim that no test can provide documentation of a loss of all neuronal functions for the definition of brain death, therefore confirmatory tests are useless<sup>15</sup>. In Europe there is fairly uniform agreement regarding the criteria for the clinical evaluation of brain death, although there is considerable variation in the use of additional confirmatory tests accepted by law and in their interpretative criteria.

We believe that caution is needed in this important matter, and that the law should guarantee for life as indeed the Italian law does. However, improvement is always possible: if the mere filling of intracranial arteries does not indicate the adequacy of perfusion, the study of the venous phase could improve the sensitivity of CTA leaving no room for individual interpretation, which could cause serious ethical concerns.

The discrepancy between CTA and TCD results in our cases points out a methodology limitation that could be overcome both, by updating Italian legislation according to other European Countries legislation such as French or Spanish, or by performing ancillary tests evaluating cerebral perfusion rather than cerebral flow. Italian law accepts cerebral scintigraphy to evaluate cerebral perfusion. The main limitations of its use are the scarce

availability, the longer duration of the exam and the associated risk and difficulty of transporting the unstable BD patient to the nuclear medicine suite. CTA is preferred because of its accessibility, simplicity, widespread use, ease of interpretation and reproducibility.<sup>9,11</sup>

### **Conclusions**

Acknowledging the existing limitations in this field, we are still far from the perfect tool to assess complete neuronal death. Nevertheless, further research validating current or evolving techniques of brain blood flow imaging can improve their diagnostic sensitivity and specificity.

### **Key messages**

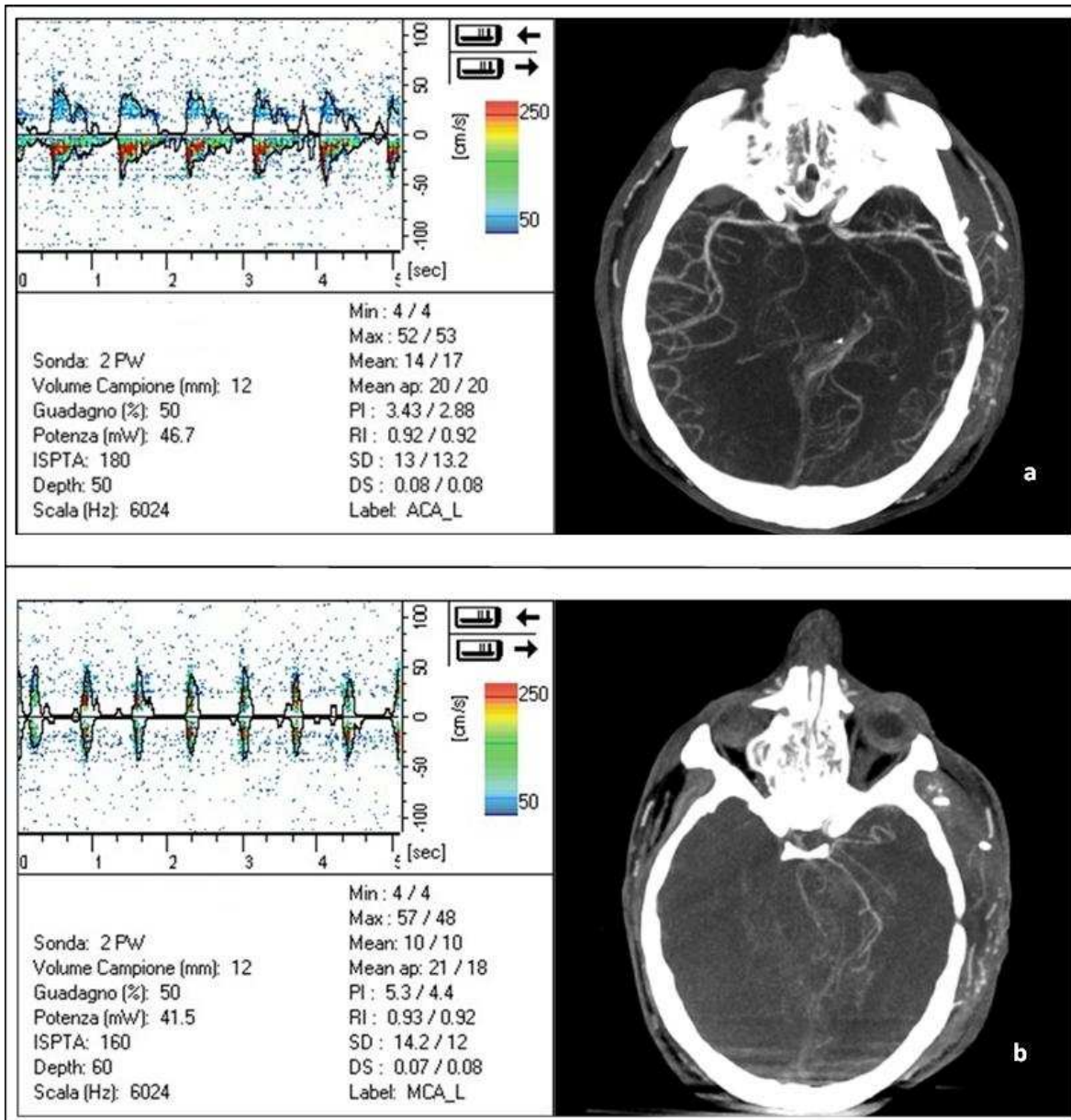
1. In cases of skull defects such as decompressive craniectomy, the increase in ICP may partially be compensated for, therefore CTA to detect CCA may lead to false-negative results, showing opacification of intracranial arteries.
2. This limitation can be overcome by the study of the deep cerebral venous flow by TCA, as suggested by the legislation of other European countries.
3. The study of the venous phase could improve the sensitivity of CTA leaving no room for individual interpretation.
4. The eventual updating of Italian legislation could help to increase the rate of organ procurement in our country.



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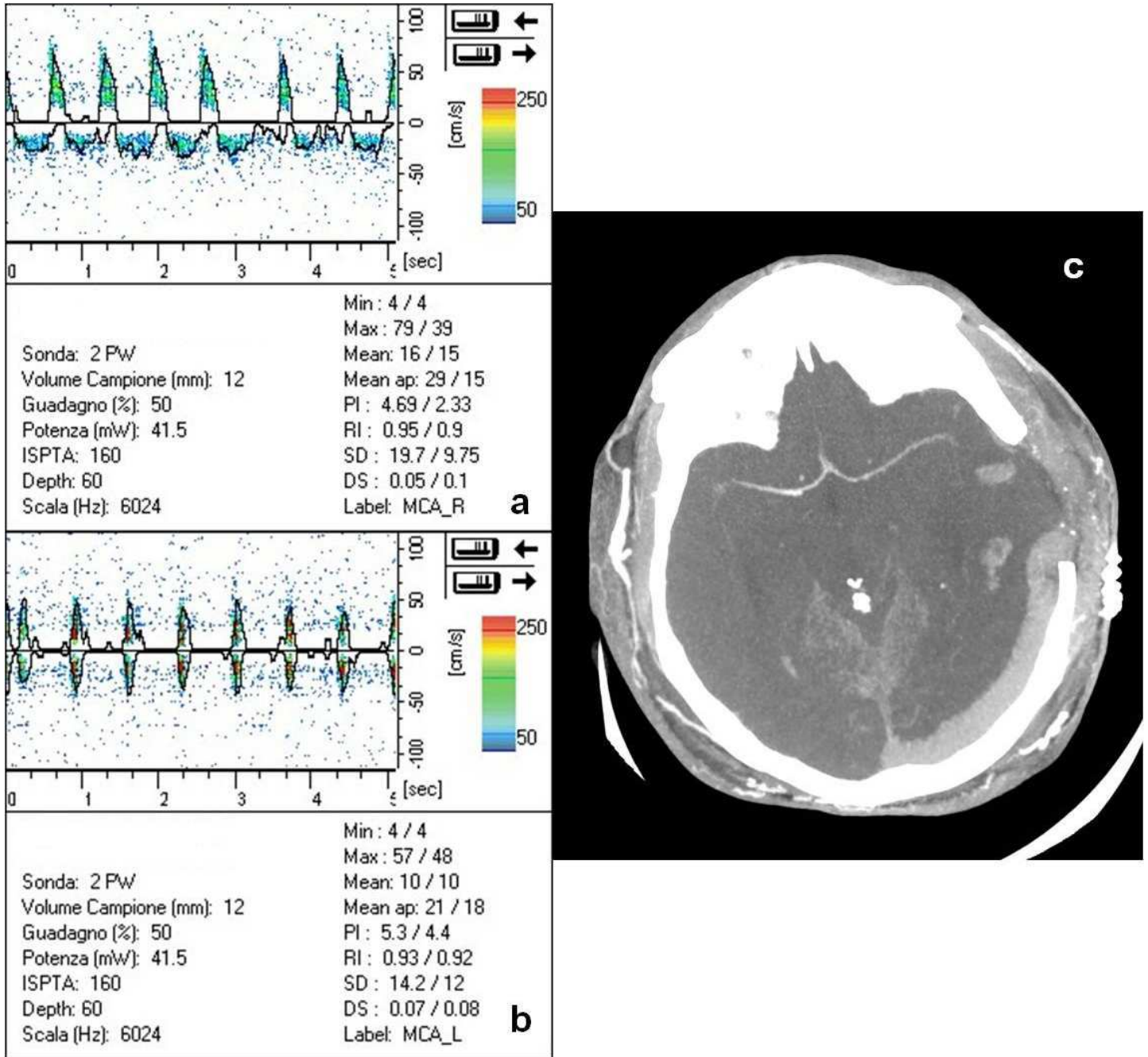
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**Figure 1 (a-b):** Transcranial Doppler (TCD) and CT-Angiography (CTA) in Patient 1 with left decompressive craniectomy.

- a) Both Transcranial Doppler (TCD) and CT-Angiography (CTA) showed intra-cerebral blood flow.
- b) TCD showed bidirectional flow on left MCA level; CTA performed 4 hours later showed internal carotid artery (ICA) and MCA opacification on the side of craniectomy (left). On the right side the exam detected the absence of filling of the intracranial arteries.



**Figure 2 (a-c):** Transcranial Doppler (TCD) and CT-Angiography (CTA) in Patient 2 with left decompressive craniectomy.

- a)-b): TCD showed bidirectional flow on both right (a) and left (b) MCAs.
- c) CTA performed few hours later showed bilateral opacification of MCAs