Imaging of Irreversible Loss of Brain Function

Bildgebende Verfahren zur Diagnostik des irreversiblen Hirnfunktionsausfalles

Authors H. Lanfermann[1], O. Schober[2]

Affiliations
[1] Institute of Diagnostic and Interventional Neuroradiology, Hannover Medical School, Germany
[2] Department of Nuclear Medicine, University Hospital Münster, Germany

Key words
- brain death
- brain perfusion
- scintigraphy
- quality control
- CT angiography

received 14.7.2015
accepted 25.9.2015

Bibliography
DOI http://dx.doi.org/10.1055/s-0041-108202
Published online: 1.12.2015
Fortschr Röntgenstr 2016; 188: 23–26 © Georg Thieme Verlag KG Stuttgart · New York · ISSN 1438-9029

Correspondence
Prof. Heinrich Lanfermann
Institut für Diagnostische und Interventionelle Neuroradiologie, Medizinische Hochschule Hannover
Carl-Neuberg-Straße 1
30625 Hannover
Germany
Tel.: ++ 49/5 11/5 32 66 54
Fax: ++ 49/5 11/5 32 58 76
Lanfermann.Heinrich@mh-hannover.de

Abstract

The updated guidelines for the determination of irreversible loss of brain function include a substantial innovation, i. e., the use of CT angiography as a supplementary technical examination. Adherence to a standardized protocol is the prerequisite for the application of CT angiography. The guidelines for standardized execution of perfusion scintigraphy are unchanged and still valid. Requirements regarding the quality of examining physicians are specified.

Key points:
- The guidelines for determining irreversible loss of brain function were updated.
- The approval of CT angiography as a supplementary examination method is a major innovation.
- CT angiography is to be performed to determine the cessation of cerebral blood circulation according to a standard protocol.
- The guidelines for the standardized implementation of perfusion scintigraphy continue to be valid.
- Quality requirements regarding examining physicians were specified.

Citation Format:
- Lanfermann H, Schober O. Imaging of Irreversible Loss of Brain Function. Fortschr Röntgenstr 2016; 188: 23–26

Zusammenfassung

In den aktualisierten Richtlinien zur Feststellung des irreversiblen Hirnfunktionsausfalles wird als wesentliche Neuerung die CT-Angiografie als ergänzendes apparatives Untersuchungsverfahren zugelassen. Voraussetzung für den Einsatz der CT-Angiografie ist die Einhaltung eines Standardprotokolls. Die Richtlinien zur standardisierten Durchführung der Perfusionsszintigrafie sind unverändert fortgeschrieben. Die Qualitätsanforderungen der untersuchenden Ärzte werden präzisiert.

Introduction

The fourth update of the guidelines regarding the determination of the irreversible loss of total function of the cerebrum, the cerebellum, and the brain stem came into effect on 7/6/2015 [1]. In compliance with the legal mandate according to § 16 Para. 1 Pg. 1 No. 1 of the Transplantation Act, these guidelines define the current state of medical science regarding the rules for determining death according to § 3 Para. 1 Pg. 1 No. 2 of the Transplantation Act and the rules for determining the irreversible loss of total function of the cerebrum, the cerebellum, and the brain stem according to § 3 Para. 2 No. 2 of the Transplantation Act including the required qualifications of physicians. They replace the guidelines from 1998 [2]. Written statements from different professional associations including the German Society of Neuroradiology (DGNR) and the German Society for Nuclear Medicine (DGN) were taken into consideration. A clear change is the replacement of the previously used term “brain death” with the more precise term “irreversible loss of brain function”.

An irreversible loss of brain function is usually the result of the cessation of cerebral blood circulation. If the cessation of cerebral blood circulation is detected, potentially reversible causes of clinical symptoms of loss of brain function are excluded. Therefore, the irreversibility of a loss of brain function can be determined without a wait time and follow-up clinical examinations. Methods such as Doppler/duplex ultrasound, perfusion scintigraphy, and CT angiography are used for this

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

purpose. As in the previous guidelines, the indication for selective arterial angiography (DSA) requires the possibility of therapeutic consequences.
This article is limited to the use of radiological and nuclear medicine imaging to determine the presence of irreversible loss of brain function. Special diagnostic features before and at the start of the third year of life are taken into consideration in the guidelines.

Radiology

In addition to the description of the necessary qualifications of independent diagnosticians, the approval of CT angiography (CTA) as a supplementary examination method is a major innovation. As in the subsequently described nuclear medicine methods, use of CTA in radiology and neuroradiology requires a standardized procedure with competent evaluation.
The pathophysiological basis of the cessation of cerebral blood circulation is an increase in the intracranial pressure above the mean arterial pressure. Cerebral perfusion then ceases so that the brain has an insufficient metabolic supply. Dupas et al. [3] studied and confirmed the reliability of CT angiography for determining the cessation of cerebral blood circulation in a large study for the first time in 1998. Subsequently, CTA was approved first in France and then in Canada, Austria, and additional countries for the diagnosis of an irreversible loss of brain function ("brain death"). This study and subsequent studies [4 – 14] were subjected to a Cochrane analysis in 2014 [15]. The sensitivity for detecting the cessation of cerebral blood circulation in the case of a previous loss of brain function was 85 %. The main cause of the lack of detection in 15 % of patients was traumatic or iatrogenic opening of the cranium that prevented an increase in intracranial pressure above the mean arterial pressure. In all examinations in which the cessation of cerebral blood circulation was documented via CTA, the irreversible loss of total function of the cerebrum, the cerebellum, and the brain stem was also confirmed.
Due to the significant success of interventional stroke therapy [16, 17], CT angiography has been used nationwide in Germany in recent years to document persistent vascular occlusions. This has resulted in a qualitatively and quantitatively excellent foundation for the use of CT angiography. In contrast to a thrombotic occlusion in the case of stroke, a pathological increase in intracranial pressure does not result in a vascular occlusion. An increase in the time from intravenous contrast administration results in relatively delayed spreading of the contrast agent in the intracranial arteries, so-called "stasis filling". This very protracted spreading of contrast agent has already been observed in the case of the use of conventional intracranial angiography and must not be confused with perfusion. In addition, there are problems evaluating CT angiography scans that additionally contain a "venous" acquisition series. Therefore, as confirmed by studies by Welschehold et al. [14], it is recommended to restrict information to be diagnostically used to the arterial phase in the case of this issue. In the case of contrast enhancement of the anterior cerebral artery, middle cerebral artery, posterior cerebral artery and basilar artery, the cessation of cerebral blood circulation is not definitively proven according to the currently valid guidelines [1]. Another examination or a second clinical follow-up evaluation must then be performed after the specified wait times.
The evaluation protocols used in the studies published to date regarding the detection of the cessation of cerebral blood circulation differ significantly. Therefore, standardization was required also in the above-mentioned Cochrane review [15]. Accordingly, a protocol for a standardized CTA procedure was created with the goal of maximum safety. With respect to evaluation, a very conservative approach was selected to ensure acceptance by requesting physicians and family members of patients [1]. The scan parameters listed in **Table 1** were defined in relation to the largest German study to date regarding the use of CTA for determining the loss of brain functions [12]. The present CTA protocol must be observed exactly and must be evaluated by radiologists with many years of experience in neuroradiology, ideally by radiologists specialized in neuroradiology since the irreversible loss of total function of the cerebrum, the cerebellum, and the brain stem is also present with the detection of the cessation of cerebral blood circulation (**Fig. 1**). The evaluation of CTA scans can be very challenging in the case of subarachnoid hemorrhage and venous stasis with simultaneous pronounced brain swelling. If the protocol is followed precisely, it is possible for external specialists with the proper qualifications to evaluate CT and CTA scans.

Table 1 The following protocol is validated and to be used for adults [1].

CTA protocol for evaluating the cessation of cerebral blood circulation
requirements
– documented clinical symptoms of loss in line with the diagnosis of irreversible loss of the total function of the cerebrum, the cerebellum, and the brain stem
– mean arterial blood pressure over 60 mm Hg
unenhanced CT
– tilting of the gantry parallel to the orbitomeatal line, CT scans from the base of the skull to the vertex with 120 kV, 170 mA; reconstructed axial scans with max. slice thickness of 5 mm
CT angiography
– intravenous administration of 65 ml of contrast agent (highly concentrated) via pressure infusion injection, followed by 30 ml of an isotonic saline solution, delivery rate of 3.5 ml/sec; the start of the spiral scan of cervical vertebral body 6, scan to the vertex is performed automatically via bolus tracking 5 seconds after at least 150 HU are achieved in the common carotid artery. 120 kV; 200 mA; table advance is: 4 cm/sec
– subsequent reconstruction of axial scans with a slice thickness of 2 mm; CT scans in units with the so-called volume scan (from cervical vertebral body 6 to vertex) are to be started automatically via bolus tracking with a time delay of 15 seconds
findings in the case of the cessation of cerebral blood circulation
– no contrast enhancement of the M1 segments of the middle cerebral artery, the A1 segments of the anterior cerebral artery, the basilar artery, the P1 segments of the posterior cerebral artery. Stasis filling can occur in V4 segments of the vertebral artery, in the PICA (posterior inferior cerebral artery) and the distal internal carotid artery (include in finding)
– good contrast enhancement of the common carotid artery and the external carotid artery and its branches
– quality control! Detection of significant contrast enhancement of the superficial temporal artery; this indicator for correct contrast administration must be carefully checked in all examinations (**Fig. 1**)

There is currently not sufficient literature regarding persons less than 18 years of age.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

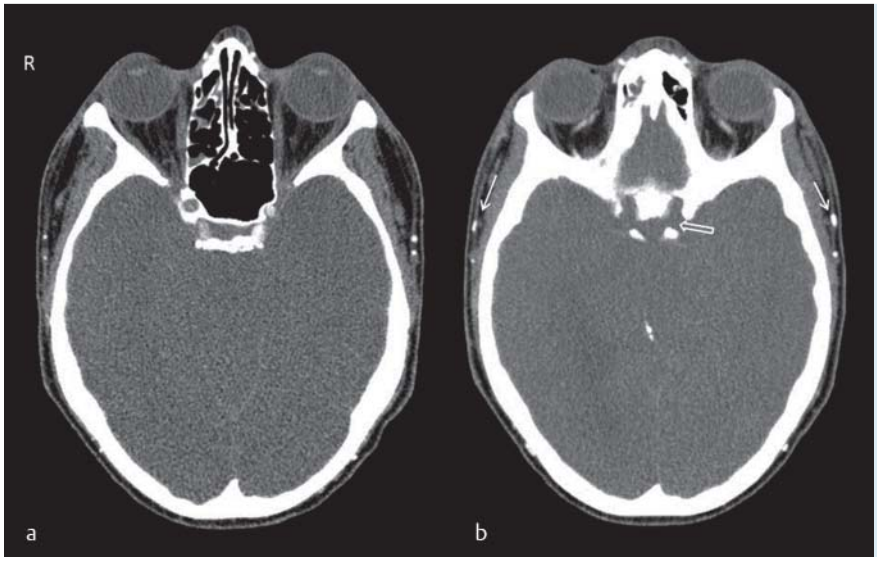

Fig. 1 Arrest of cerebral blood circulation confirmed by CT angiography. Residual contrast media inside the distal extradural internal carotid artery (ACI) (a), no contrast media inside the intradural ACI (b, open arrow). The bilateral anterior cerebral artery, middle cerebral artery, posterior cerebral artery and basilar artery showed no contrast enhancement. In comparison, good contrast enhancement (arrows) of the bilateral superficial temporal artery (quality control) is seen.

Nuclear medicine

The established procedure for performing perfusion scintigraphy in nuclear medicine has not changed since 1988 [2]. The revised guidelines emphasize the qualification requirements for examining physicians with respect to evaluation.

In perfusion scintigraphy, static scintigraphic images record the perfusion of brain tissue via a hydrophilic tracer that is metabolically actively absorbed and bound (trapped) over many hours in a virtually unchanged concentration. The lack of absorption of the radiopharmaceutical cannot be due to medication or metabolism.

Radiopharmaceuticals whose diagnostic reliability has been validated, such as Tc-99m-ethyl cysteinate dimer (ECD) and Tc-99m-hexamethylpropyleneamine oxime (HMPAO), must be used. Sufficiently substantiated studies regarding the use of biomarkers used in positron emission tomography are not currently available [19].

Different scintigraphic views must be documented. SPECT can also be performed. After bolus injection of the radiopharmaceutical, the large cranial vessels are initially visualized from a ventral direction and then static scintigraphy is performed to record tissue perfusion.

Lateral projections are required to ensure the reliability of perfusion examinations in the vertebrobasilar region. If there is still doubt due to overlapping of soft tissue structures, superimposition-free visualization with SPECT is necessary.

The scintigraphic criteria of an irreversible loss of brain function are a lack of visualization of cerebral vessels and cerebral perfusion and enhancement of the radiopharmaceutical in the brain tissue [4, 20 – 26].

Quality control should be performed in vitro by determining the labeling yield (ideally greater than 90 %) via thin layer chromatography. In addition, the physiological distribution of the radiopharmaceutical should be checked by scintigraphy of the thorax and abdomen as an in vivo quality control.

Perfusion scintigraphy must be monitored and evaluated by a nuclear medicine specialist.

References

1 Beschluss der Bundesärztekammer über die Richtlinie gemäß § 16 Abs. 1 S. 1 Nr. 1 TPG für die Regeln zur Feststellung des Todes nach § 3 Abs. 1 S. 1 Nr. 2 TPG und die Verfahrensregeln zur Feststellung des endgültigen, nicht behebbaren Ausfalls der Gesamtfunktion des Großhirns, des Kleinhirns und des Hirnstamms nach § 3 Abs. 2 Nr. 2 TPG, Vierte Fortschreibung. Dtsch Arztebl 2015; 112: A-1256/B-1052/C-1024

2 Richtlinien zur Feststellung des Hirntodes. Dritte Fortschreibung 1997 mit Ergänzungen gemäß Transplantationsgesetz (TPG). Deutsches Ärzteblatt 1998; 95: A-1861

3 *Dupas B, Gayet-Delacroix M, Villers D et al.* Diagnosis of brain death using two-phase spiral CT. Am J Neuroradiol 1998; 19: 641 – 647

4 *Berenguer CM, Davis FE, Howington JU.* Brain death confirmation: comparison of computed tomographic angiography with nuclear medicine perfusion scan. J Trauma 2010; 68: 553 – 559

5 *Bohatyrewicz R, Sawicki M, Walecka A et al.* Computed tomographic angiography and perfusion in the diagnosis of brain death. Transplant Proc 2010; 42: 3941 – 3946

6 *Combes JC, Chomel A, Ricolfi F et al.* Reliability of computed tomographic angiography in the diagnosis of brain death. Transplant Proc 2007; 39: 16 – 20

7 *Frampas E, Videcoq M, de Kerviler E et al.* CT angiography for brain death diagnosis. Am J Neuroradiol 2009; 30: 1566 – 1570

8 *Escudero D, Otero J, Marques L et al.* Diagnosing brain death by CT perfusion and multislice CT angiography. Neurocrit Care 2009; 11: 261 – 271

9 *Leclerc X, Taschner CA, Vidal A et al.* The role of spiral CT for the assessment of the intracranial circulation in suspected brain-death. J Neuroradiol 2006; 33: 90 – 95

10 *Qureshi AI, Kirmani JF, Xavier AR et al.* Computed tomographic angiography for diagnosis of brain death. Neurology 2004; 62: 652 – 653

11 *Rieke A, Regli B, Mattle HP et al.* Computed tomography angiography (CTA) to prove circulatory arrest for the diagnosis of brain death in the context of organ transplantation. Swiss Med Wkly 2011; 141: w13261

12 *Welschehold S, Boor S, Reuland K et al.* Technical aids in the diagnosis of brain death-a comparison of SEP, AEP, EEG, TCD and CT angiography. Dtsch Arztebl Int 2012; 109: 624 – 630

13 *Welschehold S, Kerz T, Boor S et al.* Detection of intracranial circulatory arrest in brain death using cranial CT-angiography. Eur J Neurol 2013; 20: 173 – 179

14 *Welschehold S, Kerz T, Boor S et al.* A. Computed tomographic angiography as a useful adjunct in the diagnosis of brain death. J Trauma Acute Care Surg 2013; 7: 1279 – 1285

15 *Taylor T, Dineen RA, Gardiner DC et al.* Computed tomography (CT) angiography for confirmation of the clinical diagnosis of brain death. Cochrane Database SystRev 2014; 3: CD009694

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

16 *Berkhemer OA*, *Fransen PS*, *Beumer D*. MR CLEAN Investigators. *et al.* A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015; 372: 11 – 20
17 *Saver JL*, *Goyal M*, *Bonafe A*. SWIFT PRIME Investigators. *et al.* Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke. N Engl J Med 2015; 372: 2285 – 2295
18 ACR Practice Guideline for the performance of single photon emission computed tomography (SPECT) brain perfusion and brain death studies. ACR Practice Guidelines and Technical Standards. Res 2007; 21: 823 – 828
19 *Bender A*, *Jox RJ*, *Grill E et al.* Persistent vegetative state and minimal conscious stae. Dtsch Arztebl Int 2015; 112: 235 – 242
20 *Bertagna F*, *Barozzi O*, *Puta E et al.* Residual brain viability, evaluated by (99m)Tc-ECD SPECT, in patients with suspected brain death and with confounding clinical factors. Nucl Med Commun 2009; 30: 815 – 821
21 *Donohoe KJ*, *Agrawal G*, *Frey KA et al.* SNM practice guideline for brain death scintigraphy 2.0. J Nucl Med Technol 2012; 40: 198 – 203
22 *Galaske RG*, *Schober O*, *Heyer R*. Tc-99m-HM-PAO and I-123-amphetamine cerebral scintigraphy: a new noninvasive method in determination of brain death in children. Eur J Nucl Med 1988; 14: 446 – 452
23 *Kim AC*, *Colletti PM*. Perfusion „brain death" scintigraphy in traumatic and hypoxic cerebral insults: correlation with CT. Clin Nucl Med 2012; 37: 880 – 888
24 *Schober O*, *Galaske RG*, *Heyer R*. Determination of brain death mit 123IMP and 99mTc-HM-PAO. Neurosurg Rev 1987; 10: 19 – 22
25 *Sinha P*, *Conrad GR*. Scintigraphic confirmation of brain death. Semin Nucl Med 2012; 42: 27 – 32
26 *Weckesser M*, *Schober O*. Brain death revisited: utility confirmed for nuclear medicine. Eur J Nucl Med 1999; 26: 1387 – 1391

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.