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 determination.

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
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].

<table>
<thead>
<tr>
<th>CTA protocol for evaluating the cessation of cerebral blood circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>requirements</td>
</tr>
<tr>
<td>– 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</td>
</tr>
<tr>
<td>– mean arterial blood pressure over 60 mm Hg</td>
</tr>
<tr>
<td>– unenhanced CT</td>
</tr>
<tr>
<td>– 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</td>
</tr>
<tr>
<td>CT angiography</td>
</tr>
<tr>
<td>– 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</td>
</tr>
<tr>
<td>– 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</td>
</tr>
<tr>
<td>findings in the case of the cessation of cerebral blood circulation</td>
</tr>
<tr>
<td>– 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)</td>
</tr>
<tr>
<td>– good contrast enhancement of the common carotid artery and the external carotid artery and its branches</td>
</tr>
<tr>
<td>– 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)</td>
</tr>
</tbody>
</table>

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

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.
19 Bender A, Jox RJ, Grill E et al. Persistent vegetative state and minimal conscious state. Dtsch Arztebl Int 2015; 112: 235–242