INTRODUCTION
The diagnosis of brain death (BD) is based on clinical criteria including deep coma, brain stem areflexia and apnoea. Depending on different local guidelines, confirmatory technical tests are sometimes mandatory. Since the 1990s, transcranial Doppler sonography (TCD) has found its place in these circumstances and fulfills most of the criteria of an ‘ideal test’ in confirming BD. To confirm intracranial circulatory arrest (CA) with Doppler sonography, typical flow patterns must be recorded in bilateral intracranial and extracranial brain-supplying arteries. A completely absent intracranial flow signal is not a reliable sign to determine CA because this can be due to transmission problems. Inadequate ultrasound penetration of the temporal bone is a major drawback of this technique, making definitive assessment of intracranial flow patterns impossible. Stabilised microbubble ultrasonic contrast agents (UCA) are routinely used in neurological clinical routine when intracranial insonation is difficult. The application of UCAs may also be helpful during BD declaration, but to our knowledge, only one publication evaluated UCAs to detect intracranial CA in BD.

MATERIAL AND METHODS
Retrospective analysis of 102 patients (46 women, 56 men), aged between 8 years and 88 years (mean: 53 years±17 years), between January 2008 and December 2011, were examined by our department. Patients were found brain dead in clinical examination and were scheduled for Doppler examination to confirm BD. Patients were suffering from different neurological diseases (intracerebral haemorrhage n=27, subarachnoid haemorrhage n=26, brain trauma n=23, hypoxic brain injury n=14, other n=12).

According to the German and international guidelines, clinical determination of BD was done by two neurointensivists. For the examination of extracranial and intracranial brain-supplying arteries, we used either a Doppler system with a 2-MHz pulsed wave Doppler probe and a 4-MHz continuous wave Doppler probe (Nicolet Companion, CardinalHealth, Hoechberg or Compumedics DWL, Singen) or a Duplex-system (2–4-MHz phased array probe and 12-MHz linear array probe, Vivid S6, GE HealthCare GmbH, Munich). Supratentorial vasculature was assessed through transtemporal, posterior fossa through suboccipital window. Intracranial CA was defined according to previously published guidelines.

If the TCD study was not conclusive (anterior and/or posterior circulation without demonstrable flow patterns), UCA was admitted. Therefore, we used 2.5 ml sulfurhexafluorid-suspension (SonoVue, Bracco, Konstanz, Germany), followed by bolus injection of 10 ml of isotonic saline solution. If additional application of UCA was necessary when contrast was rendered low, we used 1.5 ml of the sulfurhexafluorid-suspension again.

Patients with unstable ischaemic heart disease and severe pulmonary hypertension were excluded from UCA application. Statistical analysis was done by SPSS, V11.5.1 (IBM, Armonk, USA). Numbers of conclusive examinations without using UCAs were compared with the number of conclusive studies after application of UCAs, using McNemar $\chi^2$ test.

RESULTS
All our patients were brain dead in clinical examination, and BD was confirmed by an additional technical procedure.

In 69 of 102 patients (68%), TCD demonstrated intracranial CA and BD was pronounced.

In five out of 102 patients (5%), TCD demonstrated more than early systolic spikes or reverberating flow in one or more vascular intracranial territories. In four out of these five patients, large skull defects were present, and in one case, ventriculo-peritoneal shunting.

Two out of the 102 patients (2%) demonstrated, after application of UCAs, residual intracranial blood flow, not compatible with BD. Both patients had ischaemic brain injury. In all seven patients with residual brain blood flow, BD was pronounced after EEG, and somatosensory evoked potentials (SSEP) revealed no electrical brain activity.

In 23 out of the 102 patients (22%), one or more intracranial vascular territories could not be judged sufficiently, and UCAs were applied. Thereafter, in all these cases, intracranial CA could be determined. Details of accessible intracranial vascular territories are given in figure 1.

In three cases (3%), not all intracranial vascular territories were accessible after application of UCAs, and BD was confirmed by EEG and SSEP.

The number of conclusive TCD examinations improved from 74 to 99 patients ($p=<0.001$).

DISCUSSION
In 73% of our patients, native TCD examination allowed assessment of all intracranial vascular territories, opposed to 27% of our patients, in which not all intracranial vascular territories were accessible in native TCD examination. BD diagnosis would not have been possible without performing another confirmatory method. The application of UCAs lowered the rate of non-conclusive examinations to 3%.

In seven out of 102 patients (7%), we found a residual blood flow in the TCD examination. Residual brain perfusion has been described in up to 17% of BD patients and is associated with decompressed intracranial space and secondary brain injury, but this not only limits the use of TCD but all brain perfusion techniques. The relevance of this residual brain perfusion in BD is a topic of controversy. We feel that in these cases, irreversibility of brain function should be demonstrated by other blood-flow independent methods (eg, EEG or SSEP).

As mentioned above, one of the major disadvantages of Doppler examination in

![Figure 1 Results of transcranial Doppler sonography (TCD) examinations.](image-url)
diagnosing BD is the transmission problem which can be found in up to 20% of patients. In our study, this rate is higher than reported by other authors. This might be explained by the fact that we only analysed TCD after BD, so blood flow signals might have already been lost in several patients where they might have been detectable before the occurrence of BD. In 13 out of the 23 patients with intracranial CA in the UCA-TCD group, we had a conclusive TCD examination in advance of BD, so the detection of a no-flow pattern would be comparable with BD. In clinical routine, an examiner is often called for immediate evaluation of BD without having a previous TCD examination at hand. In these cases, the application of UCAs may improve the number of conclusive Doppler examinations, and improves the validity of determination of intracranial CA. The only UCA approved by European authorities for application in cerebrovascular disease is sulfur-hexafluorid-suspension. In our population, we never observed adverse events. UCAs, in general, are thought to be safe with a low rate of side effects.5

Stefan Welschehold,1,2 Florian Geisel,1 Christian Beyer,1 Andre Reuland,1,2 Thomas Kerz1

1Department of Neurosurgery, University Medical Centre, Johannes-Gutenberg-University Mainz, Mainz, Germany
2Department of Neurotraumatology and Neurosurgery, Asklepios Hospital Weisenfelds, Weisenfelds, Germany

Correspondence to Stefan Welschehold, Department of Neurosurgery, University Medical Centre, Johannes-Gutenberg-University Mainz, Langenbeckstr. 1, Mainz 55131, Germany; welscheh@uni-mainz.de

Contributors SW and FG designed this study, collected and analysed the data. SW, TK, AR and CB performed TCD examinations. SW wrote and TK reviewed the article.

Competing interests None.

Ethics approval Retrospective analysis. UCAs approved for diagnostic imaging in neurological patients.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Welschehold S, Geisel F, Beyer C, et al. J Neurol Neurosurg Psychiatry 2013;84:939–940. Received 4 October 2013 Revised 11 March 2013 Accepted 18 March 2013 Published Online First 12 April 2013

J Neurol Neurosurg Psychiatry 2013;84:939–940. doi:10.1136/jnnp-2012-304129

REFERENCES
Contrast-enhanced transcranial Doppler ultrasonography in the diagnosis of brain death


*J Neurol Neurosurg Psychiatry* 2013 84: 939-940 originally published online April 12, 2013
doi: 10.1136/jnnp-2012-304129

Updated information and services can be found at:
http://jnnp.bmj.com/content/84/8/939.full.html

**These include:**

**References**
This article cites 5 articles
http://jnnp.bmj.com/content/84/8/939.full.html#ref-list-1

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/