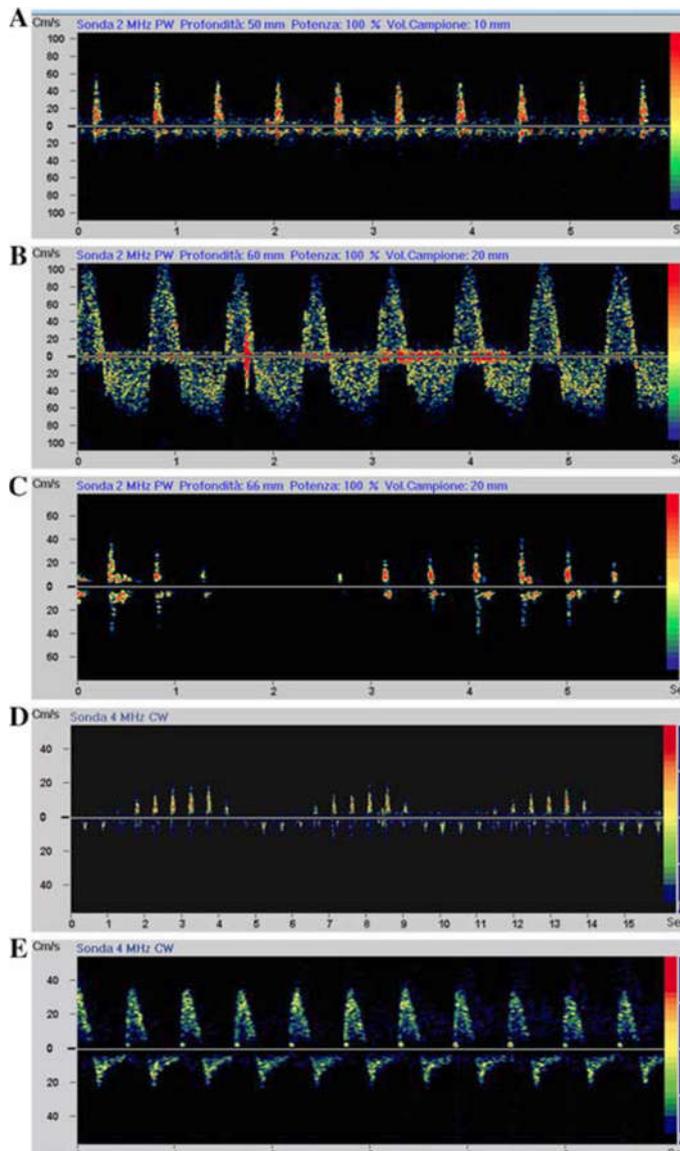


## Brain death

### Background:

Brain death (BD) diagnosis is the clinical assessment of the irreversible loss of function of the entire brain, including the brainstem. Transcranial Doppler (TCD) examination is used in several countries as a confirmatory test to assess cerebral circulatory arrest (CCA), but is not feasible in patients with absent temporal bone windows. TCD is highly specific, but less sensitive because of false-negatives results.



Typical flow patterns in CCA. (Conti u. a., 2009)

**Literature:**

**Early evaluation of critic patients possibly evolving to brain death by transcranial doppler: The role of neurosonological education and training**

<b>Author</b>	<p><i>A. Cramaro<sup>1</sup>, V. Saia<sup>1</sup>, S. Trapani<sup>1</sup>, A. Gallerini<sup>1</sup>, A. Peris<sup>2</sup>, M. Marinoni<sup>1</sup></i></p> <p><sup>1</sup> Neurosonology Lab, Department of Biomedical Sperimental and Clinical Sciences, Univesity of Florence, Italy <sup>2</sup> Intesive Care Unit, Careggi Hospital, Florence, Italy</p>
<b>Content/Summary</b>	<p>Transcranial Doppler (TCD) allows to detect diagnostic patterns of Cerebral Circulatory Arrest (CCA). Since 2003 TCD has been included by Italian guidelines of the National Transplantation Council among the techniques accepted and recommended to assess CCA in specific clinical conditions.(i.e: EEG has not a diagnostic value or cannot be performed). TCD is a time saving confirming test of BD and plays a crucial role in avoiding useless artificial life support and facilitating the organ and tissue donation procedure. TCD should be the first choice confirming test of CCA.</p> <p><b>Methods:</b> use of TCD in routine clinical practice for the early evaluation of critical patients in Intensive Care Units (ICUs). All the Neurologists and the Technicians involved in this activity got the Italian and/or the International certification in Neurosonology. All patients were daily evaluated by TCD examination since their admission in the ICUs and TCD were repeated in case of sudden changes of clinical conditions.</p>
<b>Comment</b>	<p>very important study that shows importance of TCD in ICU</p>
<b>Doppler-device</b>	<p>Not known</p>
<b>Quantification</b>	<p>Daily activity in ICUs supported by continuous training and updating led to a relevant increasing of the quality level and the amount of TCD examinations. Sensibility and specificity values in our series are in line with those published by the AAN guidelines, ranging from 91-100% and 97-100%, respectively. Up to now the lack of skilled Neurosonologists is the main cause for the limited use of TCD in BD confirming in most countries.</p>

## Coregistration of transcranial Doppler- sonography and EEG in the diagnostic procedures of detection of brain death

<b>Author</b>	<i>S. Supe, S. Hajnsek, K. Starcevic, A. Bujan Kovac</i> Department of Neurology, University Hospital Center Zagreb, School of Medicine, Zagreb, Croatia
<b>Content/Summary</b>	<p>The guidelines for the determination of cerebral circulatory arrest (brain death) include clinical criteria and, depending on countries, some confirmatory testing like TCD, EEG, Evoked potential, CT angiography, brain scintigraphy. Brain death is the process and its confirmation must be done with responsibility and proven reliability, particularly in the situations of planned organ transplantation. In donor management protocol in our practice, after brain stem death determined by clinical examination, we perform EEG and TCD monitoring followed by brain scintigraphy and in exceptional conditions, cerebral angiography as additional diagnostic test for brain death confirmation.</p> <p><b>Methods:</b> We present a case of patient which fulfilled clinical criteria of brain death due to a massive intracerebral hemorrhage (coma, absence of brainstem reflexes, apnea) in whom we monitored EEG and TCD. Initially, on the first day of clinical proven brain death, brain scintigraphy detected only minimal signs of cerebral flow in sagittal venous sinus and cerebral angiography showed minimum sustained flow in the M2 segment of the right MCA.</p>
<b>Comment</b>	Coregistration of transcranial Doppler-sonography and EEG is reliable diagnostic approach and criteria for detection of cerebral death.
<b>Doppler-device</b>	Not known
<b>Quantification</b>	During the nine days of monitoring, persisting EEG activity was obtained on right temporoparietal regions and TCD showed blood flow in right MCA on insonation through temporal bone window. On the tenth day TCD shows a “pattern of cerebral circulatory arrest” with absence of previously demonstrated flow with short enduring systolic spikes (125ms) with low systolic velocity (35cm/sec). 16 channels EEG, recorded according to the protocol for brain death did not show any electroencephalographic activity. We confirmed brain death by all criteria and the patient entered heartbeating brain death donor program

**Latin American consensus on the use of transcranial Doppler in the diagnosis of brain death.**

<b>Author</b>	<u>Caplan GA<sup>1</sup></u> , <u>Lan Z<sup>2</sup></u> , <u>Newton L<sup>3</sup></u> , <u>Kvelde T<sup>4</sup></u> , <u>McVeigh C<sup>3</sup></u> , <u>Hill MA<sup>2</sup></u> .
<b>Content/Summary Abstract</b>	Transcranial Doppler evaluates cerebral hemodynamics in patients with brain injury and is a useful technical tool in diagnosing cerebral circulatory arrest, usually present in the brain-dead patient. This Latin American Consensus was formed by a group of 26 physicians experienced in the use of transcranial Doppler in the context of brain death. The purpose of this agreement was to make recommendations regarding the indications, technique, and interpretation of the study of transcranial ultrasonography in patients with a clinical diagnosis of brain death or in the patient whose clinical diagnosis presents difficulties; a working group was formed to enable further knowledge and to strengthen ties between Latin American physicians working on the same topic. A review of the literature, concepts, and experiences were exchanged in two meetings and via the Internet. Questions about pathophysiology, equipment, techniques, findings, common problems, and the interpretation of transcranial Doppler in the context of brain death were answered. The basic consensus statements are the following: cerebral circulatory arrest is the final stage in the evolution of progressive intracranial hypertension, which is visualized with transcranial Doppler as a "pattern of cerebral circulatory arrest". The following are accepted as the standard of cerebral circulatory arrest: reverberant pattern, systolic spikes, and absence of previously demonstrated flow. Ultrasonography should be used - in acceptable hemodynamic conditions - in the anterior circulation bilaterally (middle cerebral artery) and in the posterior (basilar artery) territory. If no ultrasonographic images are found in any or all of these vessels, their proximal arteries are acceptable to be studied to look for a pattern of cerebral circulatory arrest.
<b>Comment</b>	Important study to prove TCD to be useful tool for brain death diagnostics
<b>Doppler-device</b>	Not known
<b>Quantification</b>	A consensus on use of TCD in confirmation of cerebral circulatory arrest in Latin America

### Clinical experience with transcranial Doppler ultrasonography as a confirmatory test for brain death: a retrospective analysis.

Author	(D. Sharma u. a., 2011)
Content/Summary	Using the conventional criteria, TCD confirmed BD in a large proportion, of patients where clinical diagnosis could not be made The presence of CCA pattern in one or more major cerebral artery may be prognostic of unfavorable outcome, even when BD criteria are not satisfied. Fourteen of the 19 patients who had CCA pattern in at least one artery but did not meet all the criteria for BD were subsequently found brain dead according to SPECT/clinical criteria or suffered cardiovascular death.
Comment	90 patients. TCD waveforms and medical records of all the patients examined to confirm suspected BD between 2001 and 2007, where clinical diagnosis was not possible, were analyzed.
Doppler-device	Not known
Quantification	TCD can confirm braindeath in patients, where clinical diagnosis was not sufficient.

### Transcranial Doppler in children.

Author	(Verlhac, 2011)
Content/Summary	Confirmation of a clinical diagnosis of brain death by documentation of cerebral circulatory arrest (in children!)
Comment	Review
Doppler-device	Not known
Quantification	CCA diagnosis even in children

### The relevance of early TCD monitoring in the intensive care units for the confirming of brain death diagnosis.

Author	(Marinoni u. a., 2011)
Content/Summary	TCD is a safe and inexpensive tool that can be performed at the bedside, and it allows to shorten the diagnostic process of BD, which is the prerequisite for organ donation.
Comment	
Doppler-device	Not known
Quantification	TCD as a confirmatory test in deeply sedated patients to become transplantation donors.

**Letter to the Editor**  
**Early detection of brain death.**

Author	(V. K. Sharma, 2011)
Content/Summary	An early diagnosis of brain death is the key goal for a successful organ transplantation program. I believe that multi-modal assessment, including clinical examination, EEG (with bispectral index) and TCD (with vasomotor reactivity) could be one of the possible approaches with acceptable sensitivity and specificity.
Comment	In reply to Marinoni et al., 2011
Doppler-device	Not known
Quantification	Agreement with Marinoni. Combination of different techniques to allow higher accuracy in BD confirmation.

**Transcranial Doppler in brain death confirmation in clinical practice.**

Author	(Lovrencic-Huzjan u. a., 2011)
Content/Summary	As a primary test, TCD was used in 30, brain scintigraphy in 2, multislice CT angiography (CTA) in 10, and cerebral angiography in 2 patients, and the diagnosis was confirmed in 26, 3, 9 and 2 patients, respectively. In patients in whom TCD was applied, the time to confirm the diagnosis was the shortest, and in most (61 %) cerebral circulatory arrest was confirmed within 2 hours of clinical diagnosis.
Comment	30 Patients underwent TCD for BD confirmation
Doppler-device	Not known
Quantification	TCD is a favorable confirmatory test for cerebral circulatory arrest in brain death diagnosis.

**The value of transcranial Doppler sonography with a transorbital approach in the confirmation of cerebral circulatory arrest.**

Author	(Soldatos u. a., 2010)
Content/Summary	In 11 patients with failure of the transtemporal approach, CCA was confirmed by the transorbital recordings. The addition of TOD enabled 15.5% more cases of CCA to be diagnosed by TCD. Both angiography and TCD verified CCA in all cases (k = 1).
Comment	Eighty-two clinically brain-dead patients underwent 4-vessel angiography, TCD of the basilar and middle cerebral arteries, and transorbital Doppler sonography (TOD) of the internal carotid arteries.
Doppler-device	Not known
Quantification	The addition of transorbital TCD increases the efficacy of TCD in confirming CCA in BD

### Validation of transcranial Doppler in the diagnosis of brain death

Author	(Brunser u. a., 2010)
Content/Summary	The sensitivity, specificity, positive and negative predictive values for the diagnosis of brain death with TCD were 100, 96, 96.1 and 100% respectively. Positive and negative likelihood ratios for brain death were 28 and 0, respectively.
Comment	Fifty three patients were evaluated, 25 with <u>clinical</u> brain death. On 45 cases (84.9%), the interval between both evaluations (clinical and TCD) was less than one hour.
Doppler-device	PMD 100, Spencer
Quantification	TCD is a valid and useful technique for the diagnosis of brain death and can be used on complicated cases.

### Recommendations for the use of transcranial Doppler ultrasonography to determine the existence of cerebral circulatory arrest as diagnostic support for brain death.

Author	(Segura u. a., 2009), Spanish society of Neurosonology
Content/Summary	The presence of reverberating flow, systolic spikes or absence of flow in the basilar and both middle cerebral arteries observed in two examinations is highly specific for the prediction of CCA and brain death in all patients
Comment	Based on literature analysis, the authors developed guidelines for performance and interpretation of TCD in clinically brain-dead patients, in order to confirm the diagnosis. The active members of the Spanish Neurosonology Society (SONES) reviewed an initial draft, until a consensus was reached.
Doppler-device	Not known
Quantification	Spanish recommendations.

### False positive CT angiography in brain death.

Author	(Greer u. a., 2009)
Content/Summary	CTA is not a validated confirmatory test for cerebral circulatory arrest in brain death, and may be falsely positive.
Comment	Case report
Doppler-device	Not known
Quantification	CTA is not sufficient

### Transcranial Doppler ultrasonography in the assessment of cerebral circulation arrest: improving sensitivity by transcervical and transorbital carotid insonation and serial examinations.

Author	(Conti u. a., 2009)
Content/Summary	The specificity of the testing was 100%, no false-positive cases were recorded. The sensitivity of conventional TCD examination was 82.1%. The insonation of the extracranial ICA increased sensitivity to 88% allowing the detection of CCA in those patients lacking temporal windows; serial examinations further increased sensitivity to 95.6%. Nevertheless, a CCA flow patterns may appear later on those segments. Serial examinations, may be needed in those cases.
Comment	184 patients, who met clinical criteria of brain death, observed from 1998 through 2006, were retrospectively reviewed.
Doppler-device	EME TC2000-S, Überlingen, Germany and Explorer CVS, Perols, France
Quantification	The addition of insonation of the cervical ICA and of the siphon increased sensitivity of TCD.

### Transcranial Doppler ultrasonography to confirm brain death: a meta-analysis.

Author	(Monteiro u. a., 2006)
Content/Summary	CCA by TCD in the anterior and posterior circulation predicted fatal brain damage in all patients; therefore, TCD can be used to determine the appropriate moment for angiography. Further research is needed to demonstrate that CCA by TCD on repeated examination can also predict brain death in all patients.
Comment	Meta-analysis
Doppler-device	Not known
Quantification	Good sensitivity and specificity

### Comparison between transcranial color Doppler ultrasonography and angiography in the confirmation of brain death.

Author	(Poullaras u. a., 2006)
Content/Summary	TCD was a sensitive tool to diagnose BD, affording a reliable alternative examination to standard angiography.
Comment	Forty patients experienced the clinical diagnosis of brain death due to head injury in 19 cases (47.5%), cerebral hemorrhage in 11 (27.5%), subarachnoid hemorrhage in 7 (17.5%), and cerebral infarction in 3 (7.5%).
Doppler-device	Not known
Quantification	Both angiography and TCD confirmed BD in all patients.

### Sensitivity of transcranial Doppler for confirming brain death: a prospective study of 270 cases.

Author	(de Freitas und André, 2006)
Content/Summary	The sensitivity of TCD for confirming BD may be lower than previously reported, but is probably similar to that of other non-invasive methods. The specificity of TCD is close to 100%. Uniform criteria are needed for the routine use of TCD as a confirmatory test for BD. False-negative results were persistent flow in the intracranial arteries in 47 (17.4%) patients and a lack of signal in 19 (7%). A review of 16 studies showed a sensitivity of 88% and a specificity of 98% of TCD for confirming BD.
Comment	270 patients with clinical diagnosed BD
Doppler-device	TC-22 Legend; SciMed, Bristol, UK
Quantification	The specificity of TCD is close to 100%.

### Time dependent validity in the diagnosis of brain death using transcranial Doppler sonography.

Author	(Kuo u. a., 2006)
Content/Summary	TCD can be a confirmatory tool for diagnosing brain death. The validity of TCD diagnosed brain death depends on the time lapse between brain death and the performance of TCD. TCD of both the basilar artery and the MCAs showed significant consistency in brain death diagnosis.
Comment	101 comatose patients for confirmation of brain death
Doppler-device	Not known
Quantification	The sensitivity of TCD-diagnosed brain death increased with elapsed time.

### The application of transcranial Doppler in the evaluation of brain function in deeply comatose patients.

Author	(Luo u. a., 2006)
Content/Summary	68 cases were positive in the initial examination (73.9%) and 74 cases were positive after 12 h (80.4%).
Comment	Article in Chinese
Doppler-device	Not known
Quantification	Sensitivity increased with elapse of time. TCD can be an effective and objective index in the evaluation of irreversible termination of brain function.

**Diagnosis of brain death by transcranial Doppler sonography: solutions for cases of difficult sonic windows.**

Author	(Dominguez-Roldan u. a., 2004)
Content/Summary	In 10 patients, including all the cases in which it was impossible to use a temporal approach, the carotid siphon was successfully insonated, showing in all the cases the existence of a sonographic pattern compatible with cerebral circulatory arrest. It may be concluded that the use of an orbital window for exploring intracranial circulation by transcranial Doppler sonography can be a useful tool in cases of difficult sonic windows.
Comment	
Doppler-device	Not known
Quantification	Insonation of carotid siphon allows BD confirmation when insonation through the temporal bone is insufficient.

**Utility of transcranial doppler ultrasonography for confirmatory diagnosis of brain death: two sides of the coin.**

Author	(Dosemeci u. a., 2004)
Content/Summary	The sensitivity and specificity of the first TCD examination for confirmation of brain death were 70.5% and 97.4%, respectively. Eighteen patients with clinical brain death required repeat TCD examinations because of detection of forward systolo-diastolic flow or a diastolic to-and-fro flow pattern, which were not confirmatory for the diagnosis of brain death. Brain death was confirmed ultrasonographically in 12 of 18 patients in a second examination after 12.6 +/- 8.3 hours of clinical brain death, in 2 patients in a third TCD examination, and in 1 patient in a fourth examination. Three clinically brain-dead patients had died before the diagnosis was confirmed by repeat TCD examinations. The sensitivity of TCD reached 100% in our study population after the fourth examination.
Comment	Randomized study. 100 patients (61 patients with clinical brain death, and 39 control patients with Glasgow Coma Score<5) were included in the study.
Doppler-device	Not known
Quantification	The sensitivity of TCD is increased with repeat examinations and should be repeated in cases in which systolo-diastolic forward flow is demonstrated after the first TCD. TCD may prolong or shorten the time to declaration of brain death. The necessity of demonstrating cerebral circulatory arrest in patients with clinical brain death is debatable.

## **Summary:**

TCD for confirming Brain Death has a high specificity but a lack of sensitivity (about 10 to 25 % false negative). Its sensitivity may be increased due to the combination of other methods, such as EEG.

TCD can be used to confirm BD even in children.

The sensitivity of TCD-diagnosed brain death increases with elapsed time and repeat-investigations.

In case of absence of acoustic bone windows, insonation of carotid siphon may be a good alternative.

Insonation of bilateral MCA and BA seems to be a good standard to diagnose BD.

## **Experts:**

no one in particular

Sharma?

## **Literature**

Brunser A, Hoppe A, Cárcamo DA, Lavados PM, Roldán A, Rivas R, u. a. [Validation of transcranial Doppler in the diagnosis of brain death]. *Rev Med Chil* 2010; 138: 406-412.[zitiert 2011 Okt 31]

Conti A, Iacopino DG, Spada A, Cardali SM, Giusa M, La Torre D, u. a. Transcranial Doppler ultrasonography in the assessment of cerebral circulation arrest: improving sensitivity by transcervical and transorbital carotid insonation and serial examinations. *Neurocrit Care* 2009; 10: 326-335.[zitiert 2011 Nov 2]

Dominguez-Roldan JM, Jimenez-Gonzalez PI, Garcia-Alfaro C, Rivera-Fernandez V, Hernandez-Hazañas F. Diagnosis of brain death by transcranial Doppler sonography: solutions for cases of difficult sonic windows. *Transplant. Proc.* 2004; 36: 2896-2897.[zitiert 2011 Nov 29]

Dosemeci L, Dora B, Yilmaz M, Cengiz M, Balkan S, Ramazanoglu A. Utility of transcranial doppler ultrasonography for confirmatory diagnosis of brain death: two sides of the coin. *Transplantation* 2004; 77: 71-75.[zitiert 2011 Nov 29]

de Freitas GR, André C. Sensitivity of transcranial Doppler for confirming brain death: a prospective study of 270 cases. *Acta Neurol. Scand.* 2006; 113: 426-432.[zitiert 2011 Nov 14]

Greer DM, Strozyk D, Schwamm LH. False positive CT angiography in brain death. *Neurocrit Care* 2009; 11: 272-275.[zitiert 2011 Nov 29]

Kuo J-R, Chen C-F, Chio C-C, Chang C-H, Wang C-C, Yang C-M, u. a. Time dependent validity in the diagnosis of brain death using transcranial Doppler sonography. *J. Neurol. Neurosurg. Psychiatr.* 2006; 77: 646-649.[zitiert 2011 Nov 22]

Lovrencic-Huzjan A, Vukovic V, Gopcevic A, Vucic M, Kriksic V, Demarin V. Transcranial Doppler in brain death confirmation in clinical practice. *Ultraschall Med* 2011; 32: 62-66.[zitiert 2011 Okt 31]

Luo B-yan, Zhang L-ju, Jiang M-yan, Wang J-wen, Qiu Y-qing. [The application of transcranial Doppler in the evaluation of brain function in deeply comatose patients]. *Zhonghua Nei Ke Za Zhi* 2006; 45: 116-118.[zitiert 2011 Nov 22]

Marinoni M, Alari F, Mastronardi V, Peris A, Innocenti P. The relevance of early TCD monitoring in the intensive care units for the confirming of brain death diagnosis. *Neurol. Sci.* 2011; 32: 73-77.[zitiert 2011 Nov 29]

Monteiro LM, Bollen CW, van Huffelen AC, Ackerstaff RGA, Jansen NJG, van Vught AJ. Transcranial Doppler ultrasonography to confirm brain death: a meta-analysis. *Intensive Care Med* 2006; 32: 1937-1944.[zitiert 2011 Nov 14]

Poullaras J, Karakitsos D, Kouraklis G, Kostakis A, De Groot E, Kalogeromitros A, u. a. Comparison between transcranial color Doppler ultrasonography and angiography in the confirmation of brain death. *Transplant. Proc.* 2006; 38: 1213-1217.[zitiert 2011 Nov 14]

Segura T, Calleja S, Irimia P, Tembl JI. Recommendations for the use of transcranial Doppler ultrasonography to determine the existence of cerebral circulatory arrest as diagnostic support for brain death. *Rev Neurosci* 2009; 20: 251-259.[zitiert 2011 Nov 2]

Sharma D, Souter MJ, Moore AE, Lam AM. Clinical experience with transcranial Doppler ultrasonography as a confirmatory test for brain death: a retrospective analysis. *Neurocrit Care* 2011; 14: 370-376.[zitiert 2011 Okt 31]

Sharma VK. Early detection of brain death. *Neurological Sciences* 2011; 32: 985-986.[zitiert 2011 Nov 29]

Soldatos T, Karakitsos D, Wachtel M, Boletis J, Chatzimichail K, Papathanasiou M, u. a. The value of transcranial Doppler sonography with a transorbital approach in the confirmation of cerebral circulatory arrest. *Transplant. Proc.* 2010; 42: 1502-1506.[zitiert 2011 Okt 31]

Verlhac S. Transcranial Doppler in children. *Pediatr Radiol* 2011; 41 Suppl 1: S153-165.[zitiert 2011 Nov 29]

*Rev Bras Ter Intensiva.* 2014 Jul-Sep;26(3):240-52.