Clinical application of transcranial colour-coded duplex sonography – a review

Stephan G. Zipper\textsuperscript{a} and Erwin Stolz\textsuperscript{b}
\textsuperscript{a}Neurological Department of the St Katharinenkrankenhaus, Frankfurt/Main; and \textsuperscript{b}Department of Neurology, Justus-Liebig-University, Giessen, Germany

Keywords: cerebrovascular disease, transcranial colour-coded duplex sonography (TCCS), ultrasonography

Transcranial colour-coded duplex sonography (TCCS) is a new and non-invasive ultrasound application that combines both imaging of intracranial vessels and parenchymal structures at a high spatial resolution.

This manuscript reviews the clinical applications of TCCS with focus on its diagnostic abilities in acute stroke patients. Furthermore, new experimental imaging techniques are discussed.

Introduction

One-dimensional echo-encephalography (A-mode sonography) was used up to the 1970s to determine midline shift (MLS) in suspected intracranial mass lesions. However, it soon became redundant with the introduction of computed tomography and magnetic resonance tomography, as it lacked real imaging capabilities and the spatial resolution was limited.

The introduction of transcranial Doppler sonography (TCD) by Aaslid \textit{et al.} (1982) gave new impetus to neurosonology, as it provided a non-invasive real time method to study intracranial hemodynamics at the patient’s bed-side. Numerous studies highlight its value in diagnosis and follow-up in acute stroke patients.

Transcranial colour-coded duplex sonography (TCCS) is a new technical development (Berland \textit{et al.}, 1988; Furuhata, 1989; Schöning \textit{et al.}, 1989) that combines non-invasive imaging of intracranial vessels and parenchymal structures at a high spatial resolution. In this manuscript clinical applications of TCCS and new experimental developments in this field are discussed.

Technical principles

Transcranial colour-coded duplex sonography combines gray scale imaging of intracranial parenchymal structures using the echo-impulse technique and the simultaneous depiction of intracranial vessels. For insonation low-frequency (1.75–3.5 MHz) phased array transducers are used. The advantage over conventional transcranial Doppler sonography is that intracranial vascular structures can be displayed in the correct anatomical relationships to parenchymal structures, allowing thereby angle corrected flow velocity measurements. Either flow velocities can be coded dependent on the Doppler shift resulting from moving erythrocytes [frequency-based TCCS (f-TCCS)] providing informations on flow direction and velocity or by the integrated power of the back-scattered signal [power-based TCCS (p-TCCS)]. F-TCCS is less subject to motion artifacts, whereas p-TCCS provides a better signal to noise ratio, is not subject to the aliasing effects, which on the other hand may hamper the detection of stenosed vessel segments, and is independent of the insonation angle (Griewing \textit{et al.}, 1998b). p-TCCS does not display informations on the flow direction and is therefore not used as first line imaging mode. Flow velocities are determined by spectral Doppler sonography using the colour Doppler image as a guide to the correct positioning of the Doppler sample volume. To prevent inadequate measurements, angle correction should only be applied to velocity measurements when the sample volume can be located in a straight vessel segment of at least 2 cm length (Schöning and Walter, 1992; Schöning \textit{et al.}, 1993; Baumgartner \textit{et al.}, 1994).

Echo-contrast enhancing agents (ECE) facilitate TCCS diagnosis by increasing the signal to noise ratio by a factor of 1000. This is accomplished by providing a backscatter surface that increases the ultrasound reflection coefficient ($r$) to 0.99 compared with soft biological tissues with $r$ of about 0.03. In principle ECE consist of stabilized microbubbles that survive the heart–lung passage. Besides this linear improvement of ultrasound backscatter, microbubbles exhibit non-linear acoustic properties that can be exploited for new TCCS imaging techniques (Bogdahn \textit{et al.}, 1993; Otis \textit{et al.}, 1995; Cosgrove \textit{et al.}, 1998; Görtler \textit{et al.}, 1998; Nabavi \textit{et al.}, 1998; Postert \textit{et al.}, 1999a).
TCCS examination

Because the insonation planes within a specific acoustic bone window can be chosen freely, it is useful to define standard insonation planes. The most important acoustic bone window is the temporal. The temporal axial mesencephalic or orbitomeatal scanning plane (Fig. 1) is identified by the butterfly shaped hypoechogenic mesencephalon surrounded by the echogenic basal cistern, the highly echogenic sphenoid bone, and the lateral fissure as parenchymal landmarks. By upwards tilt of the transducer from the mesencephalic axial plane by 10°, the diencephalic plane is obtained. Most prominent parenchymal structures are the third ventricle, easily recognized by its hypoechogenic double reflex, and the echogenic pineal gland. In the so called ventricular plane, further parts of the ventricular system (anterior horns of the lateral ventricles, cella media) can be examined by increasing the upwards angulation of the transducer.

The mesencephalic and diencephalic planes are used for vascular diagnostics. Slight up- or downwards tilts of the transducer are necessary to follow the course of the vessel segments of the circle of Willis. Using this approach, the distal internal cerebral artery (ICA) and in most cases the carotid siphon, the mainstem (M1) of the middle cerebral artery (MCA), the A1 segment of the anterior cerebral artery (ACA), and the P1 and P2 segments of the posterior cerebral artery (PCA) can be reliably displayed. Insonation of the P1 segment can be sometimes difficult because of hypoplasia (15–40%) (Klötzsch et al., 1996). Frequently it is possible to image M2 and M3 segments of the MCA, the A2 segment of the ACA and PCA branches. By convention, in f-TCCS a system setting is chosen that codes a flow towards the probe red and away from the transducer blue, so that the ICA, M1 MCA, and P1 PCA are coded red, whereas, parts of the carotid siphon, the A1 ACA, and the P2 PCA are coded blue.

Depiction of the anterior communicating artery as an anatomical structure is not possible because of the shortness of the vessel. However, it is possible to insonate the posterior communicating artery, although its detection is often hampered by the unfavorable insonation angle nearly perpendicular to the course of the vessel. Therefore, angle correction yields unreliable results (Klötzsch et al., 1996).

Additional coronal planes can be helpful in localizing pathological processes especially in the intracranial course of the ICA. The posterior coronal plane is useful for the assessment of the P1 PCA and the distal basilar artery (BA).

In addition, examination protocols for the following venous vessels using a transtemporal insonation have been reported (Stolz et al., 1999c): the deep middle cerebral vein (dMCV), the basal vein (BV), the great cerebral vein of Galen (GCV), the straight and transverse as well as the posterior part of the superior sagittal sinus.

The transforaminal or transmucosal examination plane enables examination of the V3 and V4 segments of the vertebral artery (VA), and of the proximal and the middle-thirds of the BA (Schönig et al., 1992; Martin et al., 1994; Schulte-Altedorneburg et al., 2000) (Fig. 2). In this plane, the occipital foramen is visible as a hypoechogenic structure, whereas the clivus is depicted as an echogenic structure. The origin of the BA is located at insonation depths of about 70 mm. The
posterior inferior cerebellar artery, in most cases originating from the V4 VA, can frequently be identified by a flow direction towards the probe.

No studies have yet reported the feasibility of transorbital TCCS using United States Food and Drug Administration approved ultrasound power limits.

The transoccipital acoustic window, located about 1 cm above and paramedian to the external occipital protuberance, allows the examination of the SRS (Straight Sinus), the GCV, and the internal cerebral veins (ICV) in a sagittal scanning plane (Baumgartner et al., 1997c).

Frontal acoustic windows provide additional axial and sagittal planes for examination of the A2 and A1 ACA, M1 MCA, P1 and P2 PCA, the rostral basilar tip, and especially the posterior communicating artery, as a result of the more favorable insonation angle compared with the transtemporal insonation. Furthermore, the pericallosal artery, the ICV, the GCV, and proximal parts of the SRS can be displayed (Stolz et al., 1999d).

Normal values, reproducibility and rate of vessel identification

Sex and age-matched normal values of flow velocities of intracranial arteries, veins and sinuses, and data on the inter- and intra-observer reproducibility have been established by several investigators (Schöning et al., 1992, 1993; Baumgartner et al., 1994, 1997c; Martin et al., 1994; Krejza et al., 1999; Stolz et al., 1999c) (Table 1). They differ somewhat between the examiners. It is not yet clear, whether this is because of instrument and operator factors or by real demographic differences. Angle corrected flow velocities are higher than those without angle correction. The latter show good agreement with previously reported TCD data (Bartels, 1993). Flow velocities in the arterial as well as the venous system are higher in women than in men, and decrease with age, whereas pulsatility increases with age. Normal values are summarized in Table 1. Reference values have been established also for the size of the third and lateral ventricles (Mursch et al., 1995; Seidel et al., 1996).

The sonographic assessment of midline shift of the third ventricle in space-occupying stroke has been evaluated with an excellent agreement with computed tomography data (Mursch et al., 1995; Seidel et al., 1996; Stolz et al., 1999a).

With advancing age the temporal bone window can become smaller or even disappear, so that the rate of vessel identification declines. This effect is more prominent in women than in men. About 15% of patients cannot be examined by TCCS using the transtemporal approach because of insufficient acoustic penetration. Identification rates decline even more with advancing age for the occipital and frontal bone windows.

The ECE markedly improve vessel identification rates in patients with insufficient acoustic bone penetration.

![Figure 2](image)

**Figure 2** f-TCCS: Normal transforaminal view.

<table>
<thead>
<tr>
<th>Table 1 Systolic and enddiastolic BFV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic BFV (cm/s)</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>MCA</td>
</tr>
<tr>
<td>ACA</td>
</tr>
<tr>
<td>PCA</td>
</tr>
<tr>
<td>VA</td>
</tr>
<tr>
<td>BA</td>
</tr>
</tbody>
</table>

Values are mean (range).
windows. Among the 15% of patients with insufficient temporal bone windows the neurovascular state can be assessed sufficiently in 90% of cases after ECE application (Bogdahn et al., 1993; Otis et al., 1995; Baumgartner et al., 1997a; Postert et al., 1997, 1998, 1999a; Görtler et al., 1998; Nabavi et al., 1998).

**Clinical applications**

**Ischemic stroke**

The most important application of TCCS is the evaluation of the cerebrovascular status in stroke patients.

Using ultrasonographic methods, several studies have demonstrated the significance of the presence and severity of cerebrovascular lesions as an early predictor of functional outcome in acute stroke (Becker et al., 1991; Görtler et al., 1998; Martin et al., 1995; Nabavi et al., 1998; Postert et al., 1998). Patency of the MCA was identified as an independent predictor of early improvement. Considering this, TCCS may identify patients who might profit from thrombolysis more than others, although current thrombolytic protocols do not require knowledge of cerebrovascular lesions. Due to its bedside capability and non-invasiveness, TCCS is especially suitable for assessment of vascular lesions in acute stroke patients. Recently data of a multicenter study showed this method to be suitable for the assessment of cerebrovascular lesions in patients with acute stroke (Gerriets et al., 2000) in the setting of thrombolytic therapy. Evaluation of pathological brain perfusion using second harmonic imaging (see New Developments) may allow estimation of the final infarct size and clinical prognosis (Federlein et al., 2000).

Diagnostic criteria of intracranial vessel occlusion are the absence of colour signals and the lack of a pw-Doppler spectrum in the occluded segment, whereas other segments of the circle of Willis and parenchymal structures can be clearly shown. Further criteria are associated intracranial hemodynamical changes such as cross-flow conditions through the anterior and posterior communicating arteries. TCCS provides a similarly high diagnostic confidence for intracranial vessel occlusion than magnetic resonance angiography (Kenton et al., 1997). Even in patients with inadequate acoustic penetration, positive (PPV) and negative predictive values (NPV) for diagnosis of MCA occlusion of 86 and 100%, respectively, have been reported after application of echo-contrast enhancing agents (ECE) (Postert et al., 1999a). Collateral flow conditions can be evaluated with a high confidence compared with digital subtraction angiography (DSA) (AcoA: sensitivity 98%, specificity 100%; PcoA: sensitivity 84%, specificity 94%) without the need of compression maneuvers (Baumgartner et al., 1997b). In cases of BA occlusion, collateral flow through the PcoA towards the BA and the contralateral PCA may be detected by a reversed flow direction of the P1 PCA (Fig. 3). Recanalization of occluded intracranial vessels, either because of spontaneous lysis or thrombolytic therapy, can be monitored by TCCS at a high time resolution (Kaps et al., 1996; Mäurer et al., 1999).

In stenosed intracranial vessels, f-TCCS depicts localized aliasing phenomena. For the grading of stenoses, recently in a retrospective, angiography con-
controlled study established TCCS criteria as well as TCD criteria can be used: a local increase in the peak systolic flow velocities, post-stenotic flow disturbances with low frequency and high intensity Doppler signals. Compared with DSA as golden standard, TCCS has a high sensitivity and specificity in detecting intracranial stenoses (Baumgartner et al., 1999).

Only anecdotal reports describe the usefulness of TCCS in diagnosis and follow-up in large vessel vasculitis.

**Vasospasm**

For diagnosis of vasospasm, TCD criteria also apply to the TCCS examination. As anatomical orientation is possible with TCCS, segmental spasms may be evaluated more accurately and easier.

**Intracranial aneurysms**

The spatial resolution of TSSC prevents the detection of aneurysms of a diameter of less than 5 mm. Furthermore, aneurysms not located in the anatomical regions accessible by TCCS, or located in the distal vessel segments, and most thrombosed aneurysms are missed. Therefore, TCCS should not be used for screening purposes.

Typically, f-TCCS depicts aneurysms as round or oval structures originating from arterial segments with zones of opposite flow direction within the structure ('coffee-bean' shape).

In a series of 88 patients, 77% of aneurysms diagnosed by DSA could be identified by f-TCCS (Fischer et al., 1998). Detection rate increased to 80% by application of p-TCCS (Griewing et al., 1998a). Three-dimensional reconstruction of 2D-TCCS planes resulted in a detection rate of 97% and an agreement on size of 95% compared with DSA. Interrater correlation for 3D-TCCS was 0.96 (Klötzsch et al., 1999).

Transcranial colour-coded duplex sonography may provide a complementary imaging technique for follow-up examinations. TCCS is able to detect or exclude residual flow within aneurysms after endovascular treatment. Thrombosed aneurysms appear hyperechogenic as do Guglielmi detachable coils. In 41 of 43 coiled aneurysms the coils could be depicted as echogenic structures, in accordance with DSA TCCS excluded intra-aneurysmatic flow in 42 cases (Schuknecht et al., 1998).

**Arteriovenous malformations (AVM)**

Typically, in f-TCCS AVMs are structures with a mosaic-like appearance in colour-mode, because of the convolution of vessels with different flow directions. In B-mode the lesion appears echogenic. Indirect diagnostic criteria are increased peak-systolic and end-diastolic flow velocities and a low pulsatility in the feeding arteries as well as increased flow velocities in the draining veins.

Using these criteria, most AVMs with a diameter > 2 cm as well as about two thirds with a diameter of < 2 cm can be detected with TCCS (Baumgartner et al., 1996). After treatment the reduction of diameter or changes in hemodynamic parameters can be assessed. However, TCCS is not able to exclude an AVM (Klötzsch et al., 1995; Schuknecht et al., 1998).

**Cerebral venous thrombosis (CVT)**

The sensitivity of TCCS in detecting CVT is currently under investigation (Stolz et al., 1999b). Indirect criteria, such as increased flow velocities in the deep cerebral veins (dMCV, BV, GCV), compensatory flow increase in the TS, and flow reversal in the GCV or SRS are found in more than 50% of cases. Direct criteria are based on a lack of colour signal in the cerebral sinuses after application of an ultrasound signal enhancer. Normalization of initially increased flow velocities concur with recanalization or effective collateralization.

**B-mode sonography, transcranial sonography (TCS)**

*Space occupying edema in acute stroke.* A major complication of hemispheric stroke is the development of a post-ischemic space-occupying brain edema that may lead to a lateral and downwards herniation of brain tissue. Lateral displacement of the third ventricle can be reliably monitored by TCS (Gerriets et al., 1999; Stolz et al., 1999a). MLS assessed by TCS in relation to the time of onset of stroke allows the prediction of a fatal outcome as early as 32 h after onset of symptoms (Gerriets et al., 1999). It may be the data that helps to decide about decompressive craniotomy, because clinical criteria alone provide limited help in this matter in the early phase of stroke. However, downwards herniation cannot be measured by TCS. Enlargement of the supratentorial ventricles can be identified as well.

*Intracerebral hemorrhage (ICH).* Acute ICH causes hyperechogenic lesions in TCS. The sensitivity and specificity for detecting supratentorial ICH by TCS are 88 and 96%, respectively (Becker et al., 1993; Seidel et al., 1993; Mäurer et al., 1998). However, infratentorial ICH, ICH < 1 cm in diameter, and cortical ICH
may be missed by TCS, so the method can not be used for exclusion of ICH. Furthermore, hemorrhagic transformation of ischemic infarcts or brain tumors appear hyperechogenic as well, so that a differential diagnosis is not possible.

Intracranial hypertension and hypotension. The value of TCS in the evaluation of the supratentorial ventricular system in space occupying stroke has already been described above. Changes of the diameter of the ventricles can be assessed by TCS with a high accuracy. However, the determination of the actual intracranial pressure (ICP) with ultrasonographic methods is still experimental. The absence of undulations of the septum pellucidum after head rotation has been proposed as a criterion of raised ICP in patients presenting with pellucidum after head rotation has been proposed as a criterion of raised ICP in patients presenting with hydrocephalus (Becker et al., 1994a). In patients with cerebral mass lesions as well as idiopathic intracranial hypertension the measurement of the optic nerve sheath (ONS) expansion by insonation through the orbit showed significantly increased ONS diameters in the patient group compared to normals (Helmke and Hansen, 1996; Salgarello et al., 1996). Recently, increased flow velocities in the superior ophthalmic vein were reported in patients with intracranial hypertension (Chen et al., 1999).

Brain tumors. They usually appears as hypoechogenic structures with a hyperechogenic rim in TCS. About 90% of intracerebral tumors can be identified by TCS (Becker et al., 1994b). Other than in computed tomography (CT) or MRI the delineation of the actual tumor mass is easier because the perilesional edema is not depicted. Therefore, TCS may be a complementary imaging method for planning of treatment and follow-up.

Neurodegenerative diseases. Transcranial colour-coded duplex sonography was the first imaging method to depict structural changes in the substantia nigra (SN) in Parkinson’s disease (PD). In several studies the echogenicity of the SN was found to be increased in PD compared with healthy normals (Becker et al., 1995). The degree of hyperechogenicity correlated closely with disease duration and severity. An increased echogenicity of the caudate nucleus has also been reported in Huntington disease (Postert et al., 1999b).

New developments

Exploiting the non-linear acoustic properties of microbubbles of ultrasound contrast enhancing agents, the development of new imaging modalities and fields of interest for TCCS is currently under way. Depending on the ultrasound power, microbubbles start to resonate and emit multiples of the fundamental frequency (Goldberg et al., 1994). These so called harmonics are unique for the microbubbles circulating in the vascular bed, however, do not occur in the brain tissue, and are basis for harmonic imaging. Harmonic imaging depicts flow signals in small and especially in the so called low flow vessels (Seidel and Kaps, 1997), that cannot be imaged with conventional TCCS modes. It is, however, hampered by the limitation of the frequency band used for insonation, as harmonic frequencies are higher and the signal intensities are lower than the fundamentals, and are therefore subject of a greater ultrasound attenuation by the skull. A further increase of transmit power induces microbubble destruction with emission of a short, energetic destruction pulse (Walker et al., 1997; Cosgrove et al., 1998). The ultrasound pulse due to bubble destruction is interpreted by the ultrasound system as flow signal (‘pseudo-Doppler’), the process itself is referred to as stimulated acoustic emission (SAE). In SAE, time and phase connection with the fundamental signal is lost, the signal only codes for the presence or absence of microbubbles. This behavior is displayed in loss of correlation (LOC) or time variance analysis (TVA) images.

Using these non-linear properties of microbubbles, the signal to noise ratio is enormously increased so that brain tissue perfusion measurements are possible. Results have been reported in healthy volunteers and stroke patients (Postert et al., 1999a; Seidel et al., 1999, 2000).

By measuring the ultrasound intensity, time–intensity curves can be calculated in different brain regions. However, problems with the quantification of brain tissue perfusion have yet to be solved.

References


colour-coded duplex sonography of cerebral arteriovenous

Baumgartner R, Mattle H, Schroth G (1999). Assessment of
> / = 50% and < 50% intracranial stenoses by transcranial

Transcranial power-based colour-coded duplex sonogra-

Gerriets T, Stolz E, Modrau E, Fiss I, Seidel G, Kaps M
(1999). Colour Doppler imaging for diagnosis of intracranial

Furuhata H (1989). New evolution of transcranial tomogra-
yphy (TCT) and transcranial colour Doppler tomography

Gerriets T, Postert T, Goertler M et al. (2000). Duplex-
sonographic assessment of the cerebrovascular status in
acute stroke. A useful tool for future stroke trials. Stroke
31:2342–2345.


Göttler M, Kross R, Bümmer M et al. (1998). Diagnostic
impact and prognostic relevance of early contrast-enhanced
transcranial colour-coded duplex sonography in acute stroke.

Transcranial power mode Doppler
duplex sonography of intracranial aneurysms. J Neuro-
imaging 8:155–158.

Griewb W, Schminke U, Motsch L, Brassel F, Kessler C
(1998b). Transcranial duplex sonography of the middle
cerebral artery stenosis: a comparison of colour-coding
techniques – frequency or power-based Doppler and con-

sonographic evaluation of optic nerve sheath expansion
under intracranial hypertension II. Patient study. Pediatr
Radiol 26:706–710.

duplex monitoring discloses hemorrhagic complications

transcranial colour-coded sonography and magnetic

Klötzsch C, Bozzato A, Lammers G, Mull M, Lennarz TB,
Noth J (1999). Three-dimensional transcranial colour-
coded sonography of cerebral aneurysms. Stroke 30:2285–
2290.

Transcranial colour-coded duplex sonography in cerebral

posterior communicating artery by transcranial colour-

Krejza J, Mariak Z, Walecki J, Szydlik P, Lewko J,
Ustymovicz A (1999). Transcranial colour Doppler
sonography of basal cerebral arteries in 182 healthy subjects: age
and sex variability and normal reference values for blood

Martin P, Evans D, Naylor A (1994). Transcranial colour-
coded sonography of the basal cerebral circulation. Refer-

ultrasound diagnosis of vascular occlusion in acute ischemic

Mäuruer M, Müllges W, Becker G (1999). Diagnosis of MCA-
occlusion and monitoring of systemic thrombolytic therapy
with contrast enhanced transcranial duplex-sonography.

between intracerebral hemorrhage and ischemic stroke by
transcranial colour-coded duplex-sonography. Stroke
29:2563–2567.

Mursch K, Vogelsang J, Zimmerer B, Ludwig H, Behnke J,
Markakis K (1995). Bedside measurement of the third
ventricle’s diameter during episodes of arising intracranial
pressure after head trauma. Using transcranial real-time
sonography for a non-invasive examination of intracranial

Nabavi D, Droste D, Kemeny V, Schulte-Alterdorndes G,
echocontrast-enhanced ultrasonography in acute stroke

transcranial imaging. Results of an American phase-two

© 2002 EFNS European Journal of Neurology 9, 1–8


List of abbreviations

ACOA = anterior communicating artery  
BFV = blood flow velocity  
ce-TCCS = contrast enhanced TCCS  
DSA = digital subtraction angiography  
ECE = echo-contrast enhancing agents  
f-TCCS = frequency-based TCCS  
MLS = midline shift  
MRA = magnetic resonance angiography  
PCOA = posterior communicating artery  
p-TCCS = power-based TCCS  
TCCS = transcranial colour-coded duplex-sonography  
TCS = transcranial sonography