# Transcranial Color-coded Sonography (TCCS): A Helpful Tool In Clinical Neurology

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**Citation**

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**Abstract**

Since its introduction by Aaslid in 1982, transcranial Doppler sonography has become firmly established both as a routine instrument for assessing the intracranial hemodynamic situation in a hospital situation and experimentally in the field of functional Doppler sonography. An extended procedure consisting of a combination of B mode and PW Doppler sonography and offering the possibility of visualizing the insonated tissue has been available since the start of the '90s as transcranial color-coded sonography (TCCS). The aim of this paper is to provide an overview of the current state of applications for TCCS from the standpoint of the hospital physician. After describing the examination procedure and values for normal populations, the paper focuses on the emergency diagnosis of patients with acute ischemic cerebral infarction within a short time after the event. The rapid differential diagnosis of stroke (within 3 hours after the onset of sym-ptoms) together with clinical data and the CT finding permits a rational decision regarding reca-nalizing therapy with t-PA. The importance of routine bedside follow-up examinations with TCCS in various indications is discussed together with their yield, patient friendliness and cost effectiveness. Finally, the paper takes a look at coming developments in the field of multidimen-sional sonography of intracranial structures.

## 1. INTRODUCTION

Before the era of computed tomography, attempts were still being made in the ‘70s to diagnose intracranial lesions with echoencephalography (A mode) by displacing the mid-line echo. With the introduction of modern computer-aided imaging procedures (CT and MRI), neurosonology receded into the background for a while. Over the last few years, however, the development of ever better ultrasound transducers, improvements in computer performance and the development of ultrasound signal enhancers have led to the reemergence of neurovascular ultrasound diagnosis.

TCD, which was introduced by Aaslid in 1982, soon found its way into every neurological clinic and is now indispensable for the diagnosis and follow-up of neurovascular diseases [$_{1}$]. TCCS with its color-coded demonstration of the frequency shift (fTCCS) or reflected energy (pTCCS) is a logical further development of TCD. However, it also offers a number of advantages and extensions because of the addition of a B image to the PW Doppler function. Thus, the classical imaging procedures are now joined by TCCS as a supplementary, noninvasive ultrasound procedure, the current clinical relevance of which is described in the following.

## 2. TECHNICAL PRINCIPLES

Transducers with transmission frequencies between 2.0 and 2.5 Mhz are used for transtemporal insonation. Either the frequency shift (fTCCS) or the energy of the Doppler signal (pTCCS) can be shown color-coded; the advantages of fTCCS consist in the demonstration of the direction and velocity of flow, those of pTCCS in the higher sensitivity particularly for lower blood flow. Demonstration of the main stems in fTCCS mode is possible in > 90% of white men over 60 years of age, but lower in women of the same age group [31]. Use of the pTCCS mode provides a distinct improvement of the sensitivity [$_{23}$]. The PW Doppler function in combination with the B image permits determination of the insonation angle and, consequently, angle-corrected measurement of the blood flow velocity (BFV). The use of echo signal enhancers (ESEs) - the principle of which is based on microspheres of air - able to survive pulmonary transit can significantly improve the sensitivity of the procedure by increasing the signal-noise ratio (approx. 20 - 30 dB). It is, for example, possible to demonstrate the main stems and segmental branches of the circle of Willis with high sensitivity and high positive (0.81) and negative (1.0) predictive value as measured against the gold standard of cDSA [$_{21}$]. The improvement of the imaging

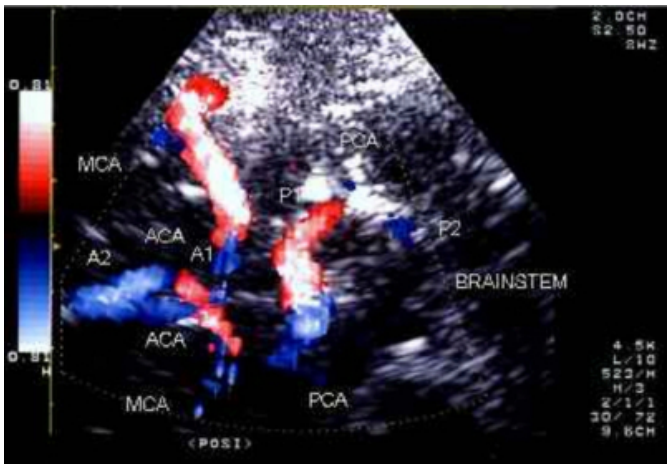
quality is dependent on the quality of the precontrast image and the concentration of the echo enhancer [32, 41]. At the present time, Levovist(tm) (Schering Inc., Germany) is the only pulmonary ESE licensed in Germany for transcranial Duplex examinations. For use in echocardiography, Optison(tm) (Mallinckrodt Inc., USA) is also licensed in Germany and the USA. Levovist(tm) is a suspension of minute (< 8 µm) bubbles of air adsorbed to galactose particles which are stabilized through the addition of a small amount of palmitic acid. Options consists of octafluoropropane-containing microspheres from heat-treated human albumin. There are also other ESEs in clinical development. Experience with the use of Levovist(tm) has shown that continuous i.v. administration with an infusion pump at rates between 0.8 and 1.7 ml/min and a concentration of 300 - 400 mg/ml is most suitable for avoiding artifacts caused by the sudden arrival on bolus injection [blooming, shadowing] and for achieving a longer duration of action

## 3. EXAMINATION PROCEDURE

The examination session is commenced with an axial projection in the orbito-meatal line through the transtemporal sound window (Fig. 1).

**Figure 1**

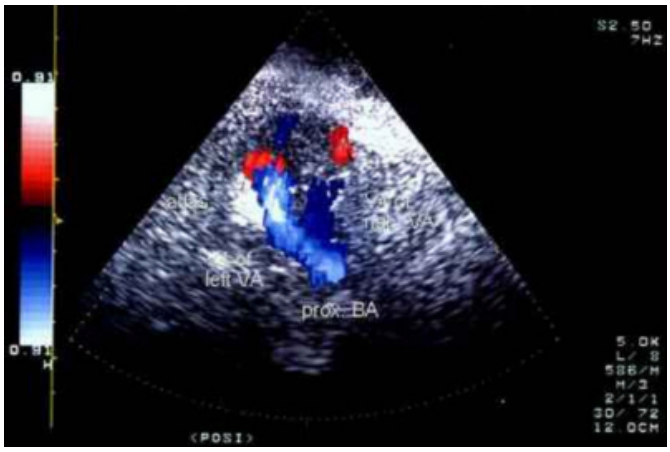
Fig. 1 Transtemporal insonation: normal findings




This projection will show the mesencephalon as a low-echo butterfly-shaped formation at a depth of about 5 - 9 cm. The mesencephalon is surrounded by a high-echo border corresponding to the basal systems. The two PCA arising from the head of the BA wrap themselves around the brain stem. Quite often, the basal vein is simultaneously insonated in the course of the P2 segment. The PcomA is sometimes also seen further rostrally. The intracranial course of the ICA with the trifurcation into the M1 segment of the MCA and the A1 segment of the ACA can invariably be seen. Demonstration of the M2 and A2 segment is often adequate only after i.v. administration of ESEs. The BFVs in all accessible main stems and possibly segment arteries are then determined. The choice of an adequate pulse repetition frequency (PRF) in fTCCS permits rapid anatomic assignment of the vessels on the basis of their direction of flow alone. Parts of the basal veins and sinuses can also be visualized at a low PRF, preferably with the help of ESEs. Tilting the transducer gives access to unusual projections with demonstration of the ventricles and the mid-line. The lateral ventricles and the thalamus are demonstrable particularly in the frontal projection. The intracranial course of the VA and the proximal segment of the BA (at a depth of about 70 - 75 mm) can be detected through the foramen magnum (Fig. 2).

**Figure 2**

Fig. 2 Transforaminal insonation: normal findings




Segments of the PICA and AICA can occasionally be seen even without administration of ESEs. The quality of the image generated is very much dependent on the thickness of the bone which, in turn, is age and sex dependent. A transtemporal projection will demonstrate the main stems of the circle of Willis in an average of 80 to 84% of cases, while a transforaminal projection will show the VA and the initial segment of the BA in 92 - 98%.

The BFVs of larger intraorbital vessels such as the ophthalmic artery (OA), the posterior ciliary artery (PCilA), the central retinal artery (CRA) and the lachrymal artery (LA) can be measured on transorbital insonation [23, 2]. The width of the optic nerve can also be determined [30, 47]. Insonation through a frontal window can occasionally lead to better demonstration of the A2 segment of the ACA and the internal cerebral vein (ICV) [55]. In some cases,

transoccipital insonation offers advantages in the demonstration of the basal veins: the middle cerebral vein (dMCV), the basal vein (BCV), Galen's veins (CVG), the straight sinus (SS) and the inferior sagittal sinus (ISS) [8].

## 4. NORMAL VALUES

Age- and sex-corrected normal values obtained in fairly large populations are available for the main stems of the intracranial arteries [36, 38]. The angle-corrected blood flow velocities as determined with TCCS are, overall, higher than the currently used values, which were obtained with TCD [4] (Tab. 1). The demonstrability of and the normal blood flow velocities found for various segments of the venous system have been reported [53]. The middle cerebral vein (dMCV), the basal vein (BCV) and Galen's veins (GCV) can, depending on the age of the subject, be demonstrated in 70 - 90% of cases, the sinus rectus (SS), the transverse sinus (TrS) and the rostral section of the superior sagittal sinus (SSS) in 55 - 70%. Maximum systolic blood flow velocities (PSV) of up to 20 cm/s are reported [53]. The BFV decreases with increasing age and is generally somewhat higher in women than in men, while the pulsatility increases with increasing age [7].

**Figure 3**

Table 1

| | | |
|---|---|---|
| MCA | 110 [100-119] | 50 [40-55] |
| ACA | 95 [80-105] | 40 [30-50] |
| PCA | 70 [55-75] | 35 [30-35] |
| VA | 55 [40-60] | 25 [20-30] |
| BA | 60 [50-70] | 35 [30-35] |

Systolische und enddiastolische Flußgeschwindigkeit (cm/sec)
[Streubreite der Mittelwerte]

## 5. CLINICAL APPLICATION

### 5.1. STROKE

The use of r-TPA appears to be an effective and rationale therapy in acute ischemic stroke [56, 27, 28], although some inconsistent results have also been reported. One possible problem is the pooling of patients with different causes of stroke. Caplan pointed out that, in respect of a good clinical outcome, it would be relevant to know the neurovascular status before beginning r-tPA thrombolysis therapy [13]. It can be assumed that thrombolysis is most effective in patients with an acute thromboembolic or thrombotic occlusion of the intracranial main stem arteries or their branches. Diagnosis and treatment have to be done within 3 (- 6) hours after the first onset of stroke symptoms. Compared to other imaging modalities TCCS can readily be used within minutes as a bedside tool in the emergency room or ICU. In the event of an insufficient transtemporal bone window (12% [40]), the application of a transpulmonary echoenhancing agent such as Levovist( (Schering Inc., Germany) provides a significant improvement in imaging quality [21, 41], leading to a definitive vascular diagnosis in 74 % [42] and showing MCA main stem and branch occlusion in 82 % [43].

Compared with CTA [20], MRA [33] and DSA [44], preliminary data show CE-TCCS to be a noninvasive diagnostic tool with findings consistent with other imaging techniques. TCCS is capable of reliably demonstrating the cerebrovascular status in acute stroke patients before and after r-tPA thrombolysis and, thus, may be used to monitor lysis therapy [39].

To date, the mortality rate of space-occupying infarctions has remained high. Early decompressive craniectomy may improve the clinical outcome [50], but the debate still continues as to who should be referred for surgery and when. Lateral midline shift (MLS) as a sign of raised intracranial pressure (ICP) can be assessed either with CT or by transtemporal B-mode insonation. Findings correlate in 90 % [52]. TCCS provides the option of bedside investigation without stressful transport of the intubated and ventilated patient to the radiology department with the impact of a further rise in ICP. On the other hand, pilot data suggest that TCCS can be helpful in selecting patients for decompressive craniotomy. MLS at 32 hours after stroke onset in patients with severe MCA infarctions may identify patients who are unlikely to survive. [22]. Nevertheless, determining the indication for decompressive craniotomy needs further evaluation.

The investigation of intracranial collateralization is routinely done with catheter angiography (cDSA). In one study (134 patients with high grade stenosis or occlusion of the ICA and 3 patients with BA occlusion), an evaluation of TCCS against cDSA by intracranial cross flow measurement TCCS showed a sensitivity of 98%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 98% for cross flow via AcomA, and of 84%, 94%, 94% and 84%, respectively, for PcomA [5]. Similar findings are seen for the detection of intracranial stenosis [6].

Significant stenoses of MCA - correlated to angiographic findings - show PSV with >180 cm/s in TCCS [34]. In another study, 9% of intracranial stenoses were missed in fTCCS compared to cDSA; however, the sensitivity can be raised by using pTCCS or CE-TCCS [26]. Preliminary data have been published concerning the aspect of the etiology of MCA stenoses. Different densities in sonography (hyperechogenic/normoechogenic) and CT (< 120 HU/>120 HU) examinations seemed to correlate well with the differentiation between atherosclerotic and thrombotic lesions by TCCS B mode [8].

## 5.2. ANEURYSM (AN) / ARTERIOVENOUS MALFORMATION (AVM) / CAROTID-CAVERNOUS FISTULA (CCF)

TCCS is not a screening method for AVM and AN, but easily allows follow-up investigation after clipping and coiling, respectively. In a series of 88 patients with 102 angiographically proven AN, 77% were detected by fTCCS [19] and 80% by pTCCS [25]. AN sensitivity was raised further on use of Levovist( in a group of 32 patients with 36 [25]. Finally, CE-3D-TCCS (30 patients) achieved a detection rate of 97%; the size of AN in TCCS correlates well with the size measured in DSA (0.95) and the interrater correlation (two skilled investigators) was found to be 0.96 [35]. Guglielmi detachable coils were identified as hyperechogenic structures in 41 of 43 coiled AN; in agreement with angiography, TCCS showed absence of flow in 42 and presence of flow in one. Monitoring of the assessment of patent artery, major branch patency and recanalization can be reliably performed with TCCS in ANs and AVMs [49]. Color coding allows identification of major feeders and venous drainage [11]. A combination of carotid duplex and TCCS provides a noninvasive method for more accurate hemodynamic study of cerebral circulation and direct imaging of carotid-cavernous fistula (CCF) [2, 15, 37].

## 5.3. SINUS VEIN THROMBOSIS (SVT) IN DEEP CEREBRAL VEINS

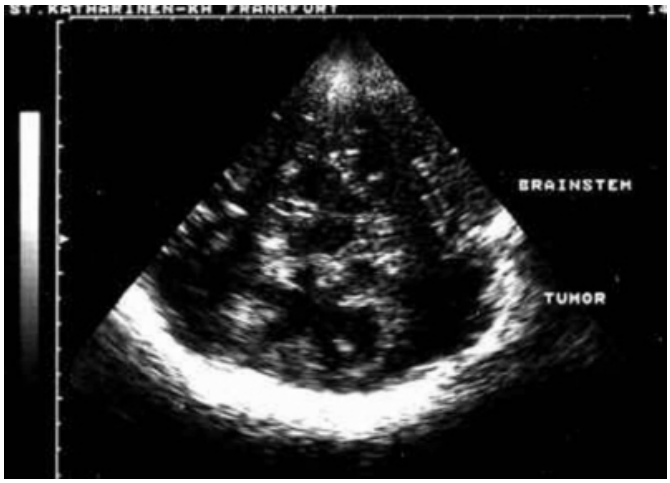
Only few data exist as yet concerning this issue. Increased BFV and side differences were demonstrated in 5 of 8 patients with MRA-verified SVT, although there was a decrease of BFV over time [54]. In 14 cases with affection of TrS at CE-TCCS, PSV was significantly decreased in hypoplastic or partially occluded vessels and increased contralaterally [46].

## 5.4. SPACE-OCCUPYING LESIONS, INTRACRANIAL HYPERTENSION AND INTRACRANIAL HYPOTENSION

Brain tissue imaging by ultrasound is now possible using the B mode. TCCS is not thought to be a first-line diagnostic tool in evaluating brain tumors, but it is valuable in the (post-op) follow-up. (Fig. 3)

**Figure 4**

Fig. 3 Glioblastoma multiforme




Vascularization of brain tumors was studied with CE-TCCS in 28 patients. All lesions were hyperechogenic with the exception of two astrocytomas. Location and extent correlated well with CT and MRI findings. Color Doppler flow signals were seen in 9/14 low-grade lesions and in 14/14 high-grade lesions. High-grade lesions always had atypical arterial and venous Doppler spectra [12]. Recent intracerebral hemorrhage (ICH) exhibited hyperechogenic signals in TCCS, while echogenicity changed to hypoechogenicity in older hemorrhage [10]. In a prospective cohort of 151 patients with ICH confirmed by CT, 12% were missed by TCCS because of insufficient bone window, 3 atypical hemorrhages were missed and 4 hemorrhages were incorrectly suspected [40].

Noninvasive assessment of ICP still remains an unresolved problem. Measurement of optic nerve sheath (ONS) expansion is possible by means of transorbital insonation. ONS diameters found in ICU patients with elevated ICP ranged to 6.8 mm and were significantly increased compared to normal (2.7 – 4.0 mm; $p<0.0007$) [31]. ONS diameters were also increased in 20 patients with idiopathic intracranial hypertension (IIH) [47]. Recently published preliminary data of 13 patients with orthostatic headache and symptoms of intracranial hypotension showed changes of maximum BFV in the superior ophthalmic vein [14]. Further

studies are needed to determine the role of TCCS in patients with changes in ICP.

### 5.5. NEURODEGENERATION

The echogenicity of the substantia nigra (SN) was increased in 12 severely affected patients with Parkinson‘s disease (PD), whereas the echogenicity of the SN in the remaining 18 patients and healthy subjects was poorly or not visualized. The degree of hyperechogenicity correlated with the severity and duration of the PD (p<0,0001). Hyperechogenicity results from nigral gliosis and reflects the stage of generation. [9]

## 6. DIAGNOSIS OF BRAIN DEATH

Brain death (BD) has been defined as the irreversible loss of function of the entire brain, including the brainstem. The American Academy of Neurology Criteria [45] include: a) loss of consciousness, b) the lack of spontaneous respiratory activity (apnea test), and, c) an isolectric EEG. The delay in the diagnosis of brain death limits organ procurement for transplantation. The goal of the TCD/TCCS is demonstrate the absence of intracranial blood flow. It may be very helpful in particular scenarios such as hemodynamic instability impeding performing the Apnea test or completing the clinical exam after traumatic brain injury. TCD/TCCS is a non-invasive study used in several countries as a confirmatory test. In BD state, cessation of blood flow within the internal carotid arteries and their branches are the typical profile. Thus, the diastolic component disappears and the sonography detects only the spike of the systolic flow. TCD/TCCS is also of special value when the therapeutic use of sedative drugs renders electroencephalography unreliable.

In the presence of open skull fractures, external drainages and craniotomies oscillating (reverberating) flow in TCCS does not constantly represent a cerebral circulatory arrest. It is absolutely necessary the presence of systolic.

There are few studies considering the sensitivity of this test. Hadani et al. [29] determined the clinical validity of the TCD in 84 BD patients. They found one clinically brain dead patients with a false negative result. In 2 of 84 cases the signals from intracranial vessels could not be obtained. On the other hand, 53 patients who did not meet the clinical criteria for brain death showed no TCD signs of total cerebral circulatory arrest. The authors conclude that specificity of the TCD test for confirmation of brain death was 100 % and the sensitivity 96.5 %.

Ducrocq et al [17] examined 130 BD patients with TCD. They found only one false negative result, in a patient with an extended skull defect, who retained TCD and angiographic intracranial circulation despite confirmed irreversible brain death. All other patients displayed typical ultrasonic patterns of cerebral circulation arrest: an oscillating signal (73%), a systolic spike (24%) or a unilateral absence of signal (n=5). No false positive result was encountered but we were unable to insonate any intracranial artery in 5 patients.

The Neurosonology Research Group (NSRG) of the World Federation of Neurology (WFN) [18] reviewed the available evidence in the literature concerning the value of TCD/TCCS in BD. This Task Force Group evaluated the role of Doppler-sonography as a confirmatory test for determining brain death. Oscillating flow or systolic spikes were defined as the typical Doppler-sonographic flow signals in the presence of cerebral circulatory arrest, which if irreversible, results in brain death.

Finally, TCCS should not be used as the unique method for determining BD diagnosis. The identification of the typical pattern requires the experience of the operator. Caution must be taken into account when interpreting the results in agreement with other diagnostic tests.

## 7. PERSPECTIVES

Apart from the already established field of use of assessing intracranial collateralization in cerebrovascular occlusive processes, (signal-enhanced) TCCS will attain special importance in future in the diagnosis of acute stroke, particularly in the selection of patients with occlusion of intracranial main stems and segment branches [43, 20, 44, 24], since the current imaging procedures are either too technical (MRA, cDSA) or demand too much computer support (CTA) or are simply not available (SPECT, PET). An international multicenter study is currently being conducted which addresses the role of TCCS in the diagnosis of stroke. Although not yet widespread, computer-aided CE-3D-TCCS permits 3-dimensional visualization of the intracranial main stems, likewise in only a few minutes. During potentially life-threatening lytic therapy, the dose of r-tPA can be controlled via the demonstration of recanalization in TCCS in order to minimize the risk of hemorrhage [39].

New insights into hemodynamics are expected from 4-D ultrasound (dynamic 3-D) in neurosonology. In 4-D imaging, ECG-triggered data acquisition of consecutive phases during the heart cycle is used to provide color-coded hemodynamic information which would otherwise be lost

[16].

In the area of cerebral tissue and, in particular, tumor demonstration, a further improvement of visualization will come from the technique of harmonic imaging and the development of new contrast agents [51].

A knowledge of the cerebral blood flow volume (global CBF) is of major importance particularly in patients on a neuro-ICU. This parameter can now be readily determined at the patient's bedside through the use of TCCS [48].

As a sensitive, quickly available and cost-effective procedure, TCCS is set to achieve a solid position in the diagnostic work-up and monitoring of many neurological emergency and intensive care patients.

## FREQUENT ABBREVIATIONS

TCCS - Transcranial color-coded sonography´

fTCCS - frequency based TCCS

pTCCS - power based TCCS

CE-TCCS - contrast enhanced TCCS

BFV - blood flow velocity

ESE - Echosignal enhancer

cDSA - catheter digital substraction angiography

MRA - magnetic resonance angiography

MLS - midline shift

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