13 TRANSCRANIAL DOPPLER

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13.1 Introduction

The study of large numbers of head-injured patients has identified clinical and radiological features which indicate the severity of the initial cerebral trauma. (Born et al., 1985; Jennett et al., 1979; Marshall et al., 1991; Miller, 1985; Miller, 1992). In some individuals, secondary neuronal injury follows the primary injury (Chan et al., 1992a; Gopinath et al., 1994; Kirkpatrick et al., 1995; Miller, 1986; Robertson et al., 1989). These secondary insults may, in part, account for the poor predictive value of early clinical findings. Until recently, the nature of secondary neuronal injury following severe head trauma has remained elusive. However, modern methods for monitoring various physical and biochemical parameters indicate that potentially adverse episodes can be detected (Bouma et al., 1992; Chan, Dearden and Miller, 1992; Chan, Miller and Dearden, 1992; Chan, Miller and Piper, 1992; Chan et al., 1992a, b; 1993; Cruz et al., 1991; Cruz, 1993; Czosnyka et al., 1994a; Jones et al., 1993; Kirkpatrick et al., 1994a, 1995, 1996; Kirkpatrick, Czosnyka and Pickard, 1996) and that some are important in terms of prognosis. Low cerebral blood flow (CBF) values in the first few hours after injury, and profound cerebral hypoxia are events which predict a poor outcome (Bouma and Muizelaar, 1990; Choksey et al., 1991; Gonalaves et al., 1994; Marion, Darby and Yonas, 1991; Meixensberger, 1993; Obrist and Wilkinson, 1990). Most importantly, they only allow isolated estimations which will miss transient secondary episodes. Their routine use in the intensive care of head-injured patients is clearly inappropriate. In response, monitors that allow the real-time estimation of cerebral pathophysiological parameters have evolved and include the continuous measurement of ICP, arterial blood pressure (BP), cerebral perfusion pressure (CPP = BP – ICP), and the indirect estimation of global cerebral oxygenation by measuring jugular venous oxygen saturation ($S_j\text{O}_2$) using jugular venous oximetry. Episodes of low CPP and $S_j\text{O}_2$ are now recognized as being detrimental (Chan et al., 1992a; Czosnyka et al., 1994a; Gopinath et al., 1994) although the exact values at which cerebral ischemia occurs probably varies with time and between individuals (Chan, Miller and Dearden, 1992). The continuous measurement of CBF for clinical application remains a goal shared by many.

Transcranial Doppler (TCD) provides a means of measuring relative changes in CBF by observing blood flow velocity (FV) in basal cerebral arteries (Aaslid, 1986; Figure 13.1), but most published data refer to the middle cerebral artery (MCA). This vessel has a favorable orientation (see below), is readily accessible to TCD insonation and provides the most reliable flow velocity signal with a that such episodes may last only a few minutes (Cruz, 1993; Kirkpatrick, Czosnyka and Pickard, 1996; Robertson et al., 1989). The need for real-time measurements is therefore apparent. The imaging methods for estimations of CBF and oxygenation using contrast agents and isotopes (xenon-enhanced CT, SPECT and PET) are invasive, and may require transfer of critical patients to specialized facilities (Bouma and Muizelaar, 1990; Choksey et al., 1991; Gonalaves et al., 1994; Marion, Darby and Yonas, 1991; Meixensberger, 1993; Obrist and Wilkinson, 1990). Most importantly, they only allow isolated estimations which will miss transient secondary episodes. Their routine use in the intensive care of head-injured patients is clearly inappropriate. In response, monitors that allow the real-time estimation of cerebral pathophysiological parameters have evolved and include the continuous measurement of ICP, arterial blood pressure (BP), cerebral perfusion pressure (CPP = BP – ICP), and the indirect estimation of global cerebral oxygenation by measuring jugular venous oxygen saturation ($S_j\text{O}_2$) using jugular venous oximetry. Episodes of low CPP and $S_j\text{O}_2$ are now recognized as being detrimental (Chan et al., 1992a; Czosnyka et al., 1994a; Gopinath et al., 1994) although the exact values at which cerebral ischemia occurs probably varies with time and between individuals (Chan, Miller and Dearden, 1992). The continuous measurement of CBF for clinical application remains a goal shared by many.

The depth and duration of secondary cerebral ischemic episode varies, and recent evidence indicates
high signal-to-noise ratio. Further, the MCA delivers approximately 70–80% of the ipsilateral carotid artery blood flow and can therefore be considered to reflect blood flow to the majority of the ipsilateral cerebral hemisphere. Bilateral real-time estimations are now available using a dual-channel facility. Most commercial machines provide analog signals with provision for digital logging, making on-line analysis of the FV signal possible and the collection of data on bedside computers convenient.

Before discussing the application of TCD in the head-injured patient, attention to the theoretical limitations of the technique and their relevance in practical terms is necessary.

For a detailed description of TCD theory, the reader is referred to the excellent descriptions provided by respected workers in the field (Newell and Aaslid, 1992a, b).

13.2 The theory of TCD sonography

13.2.1 PHYSICAL PRINCIPLES

The shift in frequency of a wave when either the transmitter or the receiver are moving with respect to the wave propagating medium was described by Doppler in 1843 and is accordingly known as the Doppler effect. The difference in frequency is known as the Doppler shift.

In a pulsed ultrasound Doppler instrument, the same transducer is used for both transmitting and receiving wave energy. The moving blood acts as a reflector, first receiving the transmitted ultrasound wave from the transducer and then reflecting the ultrasound wave back toward the transducer.

The simplified formula for the Doppler shift \( f \) from the moving blood with a velocity \( v \) is:

\[
f = 2f_0\frac{v}{c}
\]

where \( f_0 \) and \( c \) are the frequency and velocity of the emitted ultrasound wave respectively.

Insonation of the basal vessels of the circle of Willis was made possible by the development of a high frequency pulsed Doppler technique designed to penetrate skull bone. (Aaslid, Markwalder and Nornes, 1982). The frequency necessary for transcranial Doppler (TCD) applications is in the order of 2 MHz.

It is seldom that blood within a vessel is moving directly toward or away from the transducer. More generally, it will be moving in a direction at an angle of insonation to the ultrasound beam. The blood flow velocity measured using TCD is thus dependent on the angle of insonation, and can vary according to technique. For the middle cerebral artery (MCA) the error is small and of the order ±3%, since the direction of proximal segment of the MCA is such that, if extrapolated, it would meet the pterional bone at a near right angle (Figure 13.1).

Figure 13.1 Diagram showing the different anatomical locations of the basal cerebral arteries from which Doppler signals are obtained. Flow detected from the middle cerebral artery (middle trace) is towards the probe and is shown as a positive (above zero baseline) waveform. This is in contrast to the normal flow direction in the anterior cerebral artery, which is away from the probe (negative flow – upper trace). The posterior cerebral artery also produces a positive waveform.
The TCD recorded velocity varies with the real blood velocity according to the cosine of the angle of insonation. For angles of insonation between 0 and 30°, the observed velocity varies between 0.87 and 1.0 of the true velocity. The anatomical limitations for transtemporal insonation of the MCA are such that signal capture is only possible at narrow angles. Thus the observed velocity is a close approximation of true velocity at a typical depth of insonation of 5–6 cm from the scalp surface (1 cm less for children). Other anterior circulation basal vessels have a less favorable orientation, hence variation in FV derived from them is much more dependent on the technique of insonation (Figure 13.1).

13.2.2 RELATIONSHIP BETWEEN INTRACRANIAL MCA BLOOD FLOW VELOCITY AND CBF

TCD measures the velocity of red blood cell moving within a vessel. It has a single dimension per unit of time (usually quoted in cm/s). In contrast, CBF is a three-dimensional measure of volume of blood delivered per unit of cerebral tissue per unit of time (usually quoted in ml/100 g/min). The two parameters are quantitatively different; hence the correlation between absolute values of FV and CBF is poor. However, provided the cross-sectional area of the insonated blood vessel remains constant, the CBF and FV should vary directly with one another. The MCA diameter appears to be relatively constant under changing conditions of BP and carbon dioxide tension in the normal brain, as demonstrated in healthy volunteers (Aaslid et al., 1989; Dahl et al., 1989; Newell et al., 1994) thus good correlations between relative changes in FV and CBF have been reported experimentally (Barzo et al., 1991; Czosnyka et al., 1994c; Richards et al., 1995) and in clinically stable patients (Bishop et al., 1986; Romner et al., 1991). However in unstable patients with acute brain injury, the MCA diameter may be altered by changes in ICP and the effects of vasospasm, reducing the reliability of the relationship between relative CBF and FV (Kontos, 1989).

Some workers have indicated that the relationship between FV and CBF varies according to the level of CBF, with a stronger correlation occurring when CBF was low (less than 20 ml/100 g/min; Halsey, McDowell and Gelmon, 1986). These observations may reflect different states of autoregulation and a changing MCA diameter, although pressure autoregulation is believed to primarily involve the microcirculation rather than medium sized vessels. Alternatively, the flow characteristic of the formed elements may change at different flow rates, and become non-laminar at extreme values for CBF thus varying the relationship between flow and velocity. The variable relationship between absolute FV and absolute CBF is a clear disadvantage, reflected by the normal variation in MCA FV of between 35 and 90 cm/s in the awake resting state. Thus TCD demands caution in interpretation when attempting to estimate CBF from FV data in isolation of other parameters in head-injured patients.

13.3 TCD measurements

Three main pathways to access the intracranial arteries can be employed. They comprise the transtemporal approach through the thin bone above the zygomatic arch to the anterior, middle and posterior cerebral arteries and circle of Willis, the transorbital approach to the carotid siphon, and the suboccipital route to the basilar and vertebral arteries. The transtemporal approach is usually employed in critically ill patients. In expert hands, about 5% of the individuals will yield an unsatisfactory image employing the temporal window (Aaslid, 1986; Harders and Gilsbach, 1985; Harders, 1986).

Through the temporal window, the middle (MCA), anterior (ACA) and posterior (PCA) cerebral arteries can be readily examined (Figure 13.1). In each patient, the same insonation window should be used throughout the entire study period. This could be accomplished by putting a small marker at the patient’s temporal region. The Doppler examination begins with the identification of the bifurcation of the intracranial portion of the internal carotid artery into the MCA and ACA according to the method described by Aaslid (1986). This bifurcation can usually be identified at a depth of 60–65 mm. The typical Doppler signal from the carotid bifurcation is shown in Figure 13.2, which consists of images above and below the zero line of reference representing the flow directions towards and away from the ultrasound probe of the MCA and ACA respectively. The depth of insonation is then reduced to follow the upward deflection image of the MCA flow velocity as the vessel runs towards the skull. The MCA can usually be traced up to a depth of 30 mm, which is beyond the bifurcation of the MCA into the peripheral branches. The proximal portion of the main trunk of the MCA (the M1 segment) can be located at a depth of around 45–55 mm. The depth which gives the highest velocity is usually chosen for measurement. In children, the depth which gives the highest MCA velocity is usually 10 mm less than that of adults, but the same principles apply. This method of obtaining the MCA signal eliminates the possibility of mistaking the PCA for the MCA because the PCA signal cannot be obtained at a depth less than 55 mm for anatomical reasons (Aaslid, 1982; Lindegaard, 1989). Mistaking the PCA for the MCA would introduce a major error into velocity measurement due to the lower velocity of the former vessel.
After the MCA signal is obtained, the depth of insonation is increased so that the image of the carotid bifurcation can be seen again; the depth is increased further with the probe directed slightly anteriorly so that the ACA image can be found. The first part of the ACA (the A1 segment) is recognized by a direction of flow that is away from the probe. With the identification of the ACA, the depth of insonation is decreased until the carotid bifurcation signal is obtained. The probe is then angled slightly posteriorly until the signal of the PCA is seen. The PCA can be distinguished from the MCA signal by a lower flow velocity and failure to obtain the PCA signal when the depth of insonation is decreased much below 55 mm. The velocity parameters measured included the peak systolic velocity (S), end-diastolic velocity (D), the time-averaged mean velocity (M) and the pulsatility index (PI). The latter is defined as S-D/M. The timed mean velocity and PI are calculated by the Doppler machine by averaging the signals from a number of cardiac cycles by fast Fourier transformation, which eliminates error as a result of beat-to-beat and respiratory variations. Beat-to-beat variation in adults suggests that about five heart beats are adequate for measurement (Burns, 1987).

13.3.1 LONG-TERM TCD MEASUREMENT ON THE INTENSIVE CARE UNIT – PRACTICAL CONSIDERATIONS

Fixation of the probe for continuous monitoring is most conveniently achieved in the pterional region. Both solid and elasticized devices are available for probe fixation. None provide a universally accepted means of keeping the probe fixed in an identical orientation in the hostile environment of the intensive care unit. With an elasticized band we have achieved an approximately 60% signal reliability for MCA insonation in patients monitored over several days (Kirkpatrick et al., 1995). Nursing education is an essential part of this process, and it is vital to inspect the band and probe regularly to check for pressure sore development. The latter complication usually results from placement across injured scalp and bony prominences. Elasticized bands should only be applied across such areas with extreme care, since the risk of scalp swelling and necrosis is increased. The solid frame variety provides the advantage that probes can still be applied to those patients with significant scalp trauma and/or postoperative scalp flaps. However, they are bulky and cumbersome, and probe displacement is more likely during nursing maneuvers. It is clear that there is room for considerable improvement in the design of attachment devices for the purpose of long-term TCD monitoring.

The advantage of continuous monitoring is the establishment of stable baseline conditions of variables that may affect FV over intermediate periods of time. These variables include the insonation angle, arterial oxygen and CO₂ tension, blood pressure, different anesthetic agents and hemoglobin levels (Newell and Aaslid, 1992b). These concerns may be overstated, since the basal cerebral arteries, do not appear to dilate or constrict significantly with vascular resistance and/or anesthetic changes (Matta and Lam, 1995; Schregel et al., 1992, 1994). Blood pressure and
carbon dioxide tension, important determinants of cerebrovascular resistance, have little effect on the diameter of the basal arteries (Huber and Handa, 1967). Some potent vasoactive agents (e.g. sodium nitroprusside) have only a small effects on the diameter of basal cerebral vessels (Giller et al., 1993), whereas others (e.g. nitroglycerin) demonstrate significant vasodilatation (Dahl et al., 1989). While most report the diameter of the proximal MCA to be resistant to cerebrovascular variables, it would seem prudent to maintain stability during acquisition of TCD-related data. Under such stable conditions, FV changes are likely to reflect changes in CBF rather than changes in MCA diameter or technical variation.

13.4 Signal processing and data collection

13.4.1 COMPUTERS

A computer-based system is essential for logging, collating and processing the large volume of data acquired by TCD. Recognizing the changing cerebrovascular hemodynamics demands reliable monitoring techniques and sophisticated signal analysis which can only be provided by dedicated computer support (Czosnyka et al., 1994b; Kirkpatrick, Czosnyka and Pickard, 1996). Contemporary systems include sophisticated multichannel digital recorders with options for complex signal processing. The considerable flexibility of such systems permits signal analysis and presentation of information that is comprehensible to medical and nursing staff. The importance of monitoring multiple variables to increase the power of data interpretation is increasingly recognized.

13.4.2 DERIVATIVES OF FV

Signal analysis can produce large volumes of information, leading to a state of data chaos. The recording of user-defined targeted variables is therefore most desirable. Various TCD signals recorded from flow of formed elements within the MCA generate a spectrum of flow velocities that are presented as a waveform (Czosnyka et al., 1994d). The mean FV of the spectrum theoretically varies with CBF and is therefore usually presented. Since MCA flow is laminar, the maximum FV (FV_max) varies in proportion with the mean FV. Thus commercial machines take advantage of the superior signal-to-noise ratio with FV_max and calculate FV_mean from the area under the curve. The FV_max signal is frequently displayed as a FV envelope which can be resolving into FV_max during diastole (FV_d) and FV_max during systole (FV_s). It is these two components that define the pulsatility of the waveform (Figure 13.3).

13.4.3 PULSATILITY INDICES

The MCA FV waveform observed using TCD is dependent on the arterial blood pressure waveform and the viscoelastic properties of the cerebrovascular bed provided the blood rheology remains constant. Thus, if variables such as MCA diameter and BP remain constant, the pulsatility of blood flow through the conductance vessel reflects distal cerebrovascular resistance (Czosnyka et al., 1994b; Gosling and King, 1974; Lindgaard, 1992). Common determinants of changing MCA pulsatility include CO₂ tension and CCP. Several indices describing the pulsatility of blood have been formulated, the most commonly adopted is the pulsatility index (PI) of Gosling:

\[
\text{Gosling PI} = \frac{(FV_s - FV_d)}{FV_{\text{mean}}} = \frac{FV_{\text{amp}}}{FV_{\text{mean}}}
\]

The key advantage of the Gosling PI is that it is dimensionless and therefore independent of sampling techniques, provided the signal-to-noise ratio is good and the gain setting of the instrument is constant. Most TCD software packages calculate the PI index as averaged from several cardiac cycles. However, taken alone the PI cannot distinguish the cause of the flow pattern change (that is, an increase in PI can be due to cerebral vasoconstriction or to high ICP), and it needs to be interpreted in the light of other data.

Figure 13.3 Relationship between the components of FV (FV_s and FV_d) with changing CPP during a plateau wave of raised ICP and low CPP. As CPP falls, FV_d is proportionally affected to a greater extent than FV_s resulting in the divergence of these parameters, hence an increase in the pulse amplitude (FV_s minus FV_d) of the waveform is seen. CPP = cerebral perfusion pressure (mmHg); FV = middle cerebral artery flow velocity (cm/s); FV_s = FV during systole; FV_d = FV during diastole. (Source: redrawn from Czosnyka et al., 1994b.)
Figure 13.4  (a) Continuous recordings of ICP, CPP and LDF signals during waves of raised ICP in a patient with a diffuse head injury. Variations in relative CBF, estimated from FV, were closely coupled to changes in CPP indicating a state of non-autoregulation. (b) Regression analysis of the FV and LDF signal data from the period of recording shown in (a). The close correlation indicates coupling between medium vessel flow and capillary perfusion. ICP = intracranial pressure (mmHg); CPP = cerebral perfusion pressure (mmHg); FV = right middle cerebral artery flow velocity (cm/s); LDF = laser Doppler flux from the right frontal region; AU = arbitrary units. (Source: reproduced from Kirkpatrick et al., 1994a, with permission.)
Thus TCD provides a basis for cerebrovascular investigations in head-injured patients. These include the non-quantified monitoring of changing CBF, cerebrovascular autoregulatory reserve, cerebrovascular reactivity, cerebral perfusion pressure, cerebral hyperemia, post-traumatic spasm and the estimation of cerebral tamponade.

13.5 Results of analysis using TCD in head-injured patients

13.5.1 MEASUREMENT OF RAW BASELINE FV DATA

Collection of intermittent mean FV data from head-injured patients is of limited use (Chan, Miller and Dearden, 1992; Weber, Grolimund and Seiler, 1990). Chan, Miller and Dearden (1992) report that in severely head-injured patients (GCS < 8), the mean FV at admission was lower than in those with less severe head injuries. Further, the mean FV remained depressed in those same patients. However, the dispersal of data points was so wide that raw admission FV data was not a useful predictor of outcome for individuals except where very low FV was encountered (less than 28 cm/s = 80% death rate). These findings are not surprising, bearing in mind the variables that affect FV measurements in these unstable patients.

Continuous monitoring of mean FV is potentially of value when used purely as a non-quantified trend recorder, where dynamic changes from a variable baseline are considered (Kirkpatrick et al., 1994a; Kirkpatrick et al., 1995; Newell et al., 1992). Our experience in Cambridge of continuous multimodality monitoring systems, indicates that the TDC is able to detect transient changes in relative CBF with high resolution (Kirkpatrick et al., 1994a; Kirkpatrick, Czosnyka and Pickard, 1996). Thus, episodes lasting between 12 and 70 minutes were seen which corresponded to cortical cerebral perfusion changes as assessed using laser Doppler flowmetry (Figure 13.4(a)). The correlation between relative changes was high (Figure 13.4(b)) and could help to distinguish between rises in ICP associated with low CPP and those associated with hyperemia (Figure 13.5). Instances where there was significant uncoupling between FV and cortical perfusion were rare (Figure 13.6). It is the high dynamic resolution provided by TCD and the
correlation with other hemodynamic modalities that are proving encouraging to neurointensivists employing the technique as a real-time monitor.

13.5.2 AUTOREGULATION IN HEAD INJURY

Cerebral autoregulation describes the cerebrovascular reflexes that maintain CBF during changing CPP (Paulson, Olesen and Edvinsson, 1990). Failure of autoregulation, which is frequent after severe head injury, may aggravate cerebral ischemia during periods of relative poor perfusion (Miller, 1985; Siesjö, 1992). Thus the autoregulatory status of the cerebral vasculature may provide an index of injury severity, help define the cerebrovascular reserve and indicate the susceptibility of individuals to secondary ischemia during low cerebral perfusion (Marmarou et al., 1991).

Assessment of autoregulation using TCD depends on the assumption that relative changes in FV correlate with relative changes in CBF. Thus, if autoregulation is intact, FV should remain constant with a changing CPP. Conversely, if autoregulation has failed, the relation between CPP and FV becomes linear (Figures 13.3, 13.7). The value of CPP at which autoregulation

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**Figure 13.6** An abrupt rise in ICP and fall in CPP recorded during attempted withdrawal of dopamine inotropic support. Simultaneous falls in FV and LDF occurred. On recovery of CPP a transient hyperemia was registered by LDF, but not by FV, indicating uncoupling of flow in different sized vessels. ICP = intracranial pressure (mmHg); CPP = cerebral perfusion pressure (mmHg); FV = right middle cerebral artery flow velocity (cm/s); LDF = laser Doppler flux from the right frontal region; AU = arbitrary units. (Source: reproduced from Kirkpatrick et al., 1994a, with permission.)
Figure 13.7  Three characteristic patterns of linear regression between spontaneous waves of CPP and the components of the FV waveform captured over a 15 minute epoch. \( FV_m, FV_s \) and \( FV_d \) are resolved. A negative correlation between \( FV_s, FV_m, FV_d \) and CPP (left graph) indicates intact autoregulation for all components and is predictive of a favorable outcome. Disturbance of autoregulation initially affects the \( FV_d \) component (middle graph) resulting in a positive relationship between \( FV_d, FV_m \) and CPP, while \( FV_s \) remains independent of CPP. In a fully depleted autoregulatory state (right graph) all components of FV show a positive correlation with CPP, resulting in a pressure passive state. This is predictive of an unfavorable outcome. ICP = intracranial pressure (mmHg); CPP = cerebral perfusion pressure (mmHg); FV = right middle cerebral artery flow velocity (cm/s); \( FV_m \) = mean flow velocity; \( FV_s \) = FV during systole; \( FV_d \) = FV during diastole. Source: redrawn from Czosnyka et al., 1995.
fails and FV begins to fall is called the autoregulatory 'threshold' or 'break point'. Since the autoregulatory threshold is dependent on $P_{CO_2}$ levels – in states of hypercapnia the threshold is exceeded at lower levels of CPP (Markwalder et al., 1984; Paulson, Olesen and Edvinsson, 1990) – this variable has to be kept constant for repeated evaluations.

The autoregulatory status can be assessed using TCD in a variety of ways. Formal lowering of blood pressure is no longer considered ethical in the head-injured. Observing the responses to spontaneous changes in BP is an alternative (Czosnyka et al., 1994b), but such transients are infrequent, often of low magnitude, and assessments cannot be made at designated times. This is especially so in the present era of promoting a high CPP with fluid replacements and inotropes (Rosner, Rosner and Johnson, 1991). However, transient falls in CPP can be safely induced by a three second carotid compression, or for longer periods (20–30s) by inflating and releasing large blood pressure cuffs applied to the legs (Czosnyka, Pickard and Whitehouse, 1992; Giller, 1991; Smielewski et al., 1996). These indirect methods have been employed for bedside assessments, but the results are technique-dependent. Although such methods have confirmed that autoregulation is more frequently absent in the most severe head-injured patient (Chan, Miller and Dearden, 1992; Czosnyka et al., 1994e; Steiger et al., 1994; Wong, Piper and Miller, 1994), further evaluation is required.

The continuous assessment of the TCD wave profile is potentially a sophisticated way of estimating cerebral autoregulation. Thus with falling CPP, $FV_d$ will reach the autoregulatory threshold before $FV_s$, resulting in divergence of these parameters and an increase in pulse amplitude and PI (Figure 13.3). Thus a decline in $FV_s$ and an increase in PI gives an earlier warning of impending autoregulatory failure than does $FV_{mean}$. If $FV_s$ also falls with a drop in CPP, then all components of the FV waveform have reached the autoregulatory threshold, indicating a severely depleted cerebrovascular reserve. An evaluation of the gradient of linear regression between the two main components of the FV waveform ($FV_s$ and $FV_d$) and the CPP show that patients with failure of autoregulation in both components are most likely to have an unfavorable outcome when compared to those patients who have intact autoregulation or failed autoregulation in $FV_d$ alone (Figure 13.7; Czosnyka et al., 1995).

13.5.3 NON-INVASIVE ASSESSMENT OF CPP

From the above considerations, it can be seen that the different FV parameters may be used to indicate failing autoregulation. If this occurs at a consistent value of CPP between individuals, then changes in FV may provide a non-invasive estimation of CPP. The most sensitive index of falling CPP is the increase in FV amplitude due to divergence of $FV_s$ and $FV_d$ (Figures 13.3, 13.7). By calculating the PI from FV amplitude and $FV_{mean}$, an index of falling CPP is provided which is independent of the angle of insonation (Figure 13.8). Clinical experience has demonstrated a close correlation between CPP and PI. Chan et al. (1992a) demonstrated a better correlation between CPP and PI than between $FV_{mean}$ and CPP, and this relationship was independent of the mechanism of reduced CPP (hypotension or raised ICP). Two breakpoints were identified on the CPP/PI curve using sequential linear regressions: PI was independent of CPP when the latter was above 70 mmHg; between 70 and 20 mmHg the PI increased ($r = 0.767$, $p < 0.0001$, $n = 41$); and below 20 mmHg PI rose rapidly. Thus at a CPP of between 20 and 70 mmHg autoregulation is impaired but not completely exhausted. Other groups have confirmed the existence of a relationship between CPP and PI (Aaslid et al., 1986; Czosnyka et al., 1994e; Newell et al., 1993), although different breakpoints are quoted that probably reflect methodological variation (anesthetic agents and differences in the preferred level of $CO_2$ maintenance). Since the PI is dependent on BP, a standardized pulsatility index (SPI) can be calculated (SPI = PI/BP), which promises to improve the convergence of data describing the relationship between

![Figure 13.8: Relationship between the pulsatility index of the FV waveform (PI) and CPP. At high CPP values PI remains constant. At low CPP values PI increases rapidly. The exact threshold for CPP at which PI starts to increase differs among patients, and can vary in the same patient at different times. However, pooled data from different sources indicates that the threshold lies between 55 and 75 mmHg. (Source: redrawn from Czosnyka et al., 1994e.)](image-url)
CPP and pulsatility (Kirkpatrick et al., 1993). This work raises the concept of a therapeutic window existing between the completely intact autoregulatory state and the completely exhausted autoregulatory state, the equivalent of the ‘transient’ zone described in experimental animals using TCD and laser Doppler methods (Czosnyka et al., 1994c; Nelson et al., 1992; Richards et al., 1995).

Mathematical models can be generated that attempt to predict the CPP and cerebral autoregulatory status of the cerebral circulation from TCD FV waveform analysis. Aaslid and colleagues (1986) and Czosnyka et al. (1994b) have suggested different formulae relating CPP with flow velocity amplitude, flow velocity mean and BP amplitude. The difficulty encountered by these groups is that the convergence of data points from pooled patient groups is relatively low, making prediction of CPP for individuals imprecise. Further, the various thresholds described for CPP, FV and PI may vary for any patient with time (Chan, Miller and Dearden, 1992).

13.5.4 RELATIONSHIP BETWEEN TCD CHANGES AND OTHER CEREBRO-HEMODYNAMIC VARIABLES

Cerebral tissues can tolerate limited changes in CBF before metabolic requirements fail and neuronal function becomes compromised. (Wong, Piper and Miller, 1994). Thus a fall in CPP below certain thresholds results in loss of cerebral electrical activity and, on further reduction, loss of membrane stability resulting in neuronal death. Failure of pressure autoregulation does not necessarily indicate impending cell death, since the CPP threshold for pressure autoregulatory failure and metabolic failure may be different. By employing continuous multimodality monitoring techniques, the response of both CBF and cerebral metabolic variables to changing CPP can be observed in individual cases (Chan et al., 1992a; Kirkpatrick et al., 1995). Transient episodes of cerebral hypoperfusion due to hypotension or ICP plateau wave activity usually result in relative falls in CBF, and cerebral oxygenation (Figure 13.5(a)). A delay in the fall in tissue oxygenation (read with near-infrared spectroscopy and jugular venous oximetry) of approximately 2 minutes is seen after the fall in CPP, suggesting that parenchymal desaturation is secondary to the change in tissue perfusion.

By pooling intermittent data from patients in whom CPP and $S\text{O}_2$ measurements were recorded, a threshold of 71 mmHg was found below which $S\text{O}_2$ fell ($r = 0.78$, $p < 0.0001$, $n = 22$; Chan et al., 1992a). This is almost identical to the CPP threshold defined by PI (see above; Figure 13.8), suggesting that pressure autoregulatory failure defined by TCD does imply the onset of cerebral desaturation and the need for increased oxygen extraction (Figure 13.9). The precise threshold at which neuronal injury ensues has yet to be defined and awaits the identification and monitoring of products of neuronal damage in the venous effluent. Despite this, some reputable centers now advocate the maintenance of CPP above 70 mmHg, with very impressive results (Miller, 1992; Rosner, Rosner and Johnson, 1991).

13.5.5 CEREBROVASCULAR REACTIVITY IN HEAD INJURY

Cerebrovascular reactivity describes the near linear relationship between cerebral artery CO$_2$ levels and

![Figure 13.9](image-url) Composite plot of cerebral perfusion pressure (CPP) versus jugular venous oxygen saturation ($S\text{O}_2$) and doppler pulsatility index (PI) showing the CPP breakpoint of 70 mmHg.
CBF, and can be tested by observing the change in FV in response to changes in CO₂ (Dahl, 1992; Klingelhofer and Sander, 1992; Markwalder et al., 1984; Marmarou et al., 1991; Rommer et al., 1991; Schalen, Messeter and Nordstrom, 1991; Smielewski et al., 1994, 1995; Strebel et al., 1994). In normal individuals, a 1kPa increase in CO₂ causes (on average) a 22% increase in MCA FV, and thus TCD has been used to assess CO₂ reactivity in many clinical situations. Reduced or absent CO₂ reactivity indicates that the impaired CO₂ reactivity (Klingelhofer and Sander, 1992). The same appears true of head-injured patients (Grosset et al., 1993; Schalen, Messeter and Nordstrom, 1991). The use of acetazolamide, a potent cerebral vasodilator, cannot assess vasoconstriction and has not been employed in head-injured patients.

13.5.6 ABNORMALLY HIGH FV IN HEAD INJURY

Elevated levels of FV can either indicate a narrowed MCA (vasospasm or stenosis) or high CBF (hyperemia). Both vasospasm and hyperemia are well recognized following head injury (Chan, Dearden and Miller, 1992; Chan et al., 1992b; Compton and Teddy, 1987; Muttaqin et al., 1993) and since they demand a different therapeutic response their distinction is potentially important (Pickard and Czosnyka, 1993). If vasospasm is suspected, one can insonate the extracranial internal carotid FV and calculate the Lindegaard ratio (FVmca/FVica, Lindegaard et al., 1988). Vasospasm is likely when this ratio exceeds 3 (Aaslid et al., 1986). Cerebral vasospasm after severe head injury has long been recognized (Macpherson and Graham, 1973) and is frequently associated with traumatic subarachnoid blood. The flow velocities recorded in such cases are usually between 100 and 150 cm/s, hence lower than those found after aneurysmal subarachnoid hemorrhage, and the time course is also shorter, occurring within the first 2–5 days. Nevertheless, CBF can be significantly impaired with ischemic consequences (Chan et al., 1992b). Early evidence from randomized trials suggests that such patients may benefit from cerebral calcium antagonists (European Study Group, 1994).

Protracted cerebral hyperemia is also recognized following head injury, especially in children (Bruce et al., 1981; Muizelaar et al., 1989). Transient elevations in FV due to hyperemia may also occur, and can be captured with multimodality monitoring using near-infrared spectroscopy. Such episodes are accompanied by highly correlated elevations in ICP, FV, SjO₂, and total blood volume (Figure 13.5(b)). Chan et al. (1993) described a waveform notch in diastole in non-hyperemic patients with increased FV (see above). The importance of recognizing hyperemia as a cause of pathologically raised ICP is that conventional methods for treating elevated ICP (such as mannitol, and inotropes/colloid to elevate CPP) will increase CBF and worsen the intracranial hypertension.

13.6 Role of TCD in monitoring therapy

TCD allows the opportunity to observe the response of the MCA FV to different therapies (Chan et al., 1993; Eng et al., 1992; Schregel et al., 1992; Thiel et al., 1992). When therapy was instigated to improve CPP (n = 22), a linear relationship with PI (r = 0.941, p < 0.0001) and SjO₂ (r = 0.837, p < 0.0001) was seen with a CPP threshold at 70 and 68 mmHg respectively, above which the correlations disappeared (Chan et al., 1993; Figure 13.11). The real-time facility offered with a secured TCD probe is also used to monitor the dynamic response to therapy (Eng et al., 1992; Kirkpatrick et al., 1994b; Kirkpatrick, Czosnyka and Pickard, 1996; Mayberg et al., 1993; Schregel et al., 1992; Thiel et al., 1992). The response to an infusion (n = 23) of a 200 ml bolus of mannitol has been compared with that of a preceding bolus of 200 ml saline, both given over 20 minutes in 14 severely head-injured patients with raised ICP (Figure 13.12(a)). After mannitol only, a fall
in ICP (−21%) was accompanied by an increase in FV (+13%, \( p < 0.001 \)) and fall in cerebrovascular resistance (Figure 13.12(b)). The effect of mannitol on FV decayed exponentially with a time constant of 34.0 minutes (Figure 13.12(c)) and was independent of the pressure autoregulatory status of the patient (Kirkpatrick et al., 1994b; Kirkpatrick, Czosnyka and Pickard, 1996).

Although this data is of greater scientific interest than clinical relevance, the short-term manipulation of cerebrovascular hemodynamics is gaining in importance. Bearing in mind the short duration of many secondary events, continuous TCD is of use in their rapid detection and in monitoring the subsequent response to chosen therapy. This is especially important if potentially dangerous maneuvers, such as hyperventilation in states of cerebral oligemia, are to be avoided (Gold, 1989).

### 13.7 TCD in the diagnosis of brain death

From Figure 13.3 it can be seen that, as CPP falls, \( FV_d \) approaches zero and forward movement of blood only occurs during systole. When CPP falls further, a state of reverberant flow can be seen, where reverse flow occurs during diastole. It is at this point that a very high PI is seen. *Once backflow during diastole equals forward flow during systole (oscillating flow pattern), no net flow of blood occurs and cerebral tamponade in the territory of the insonated vessel is complete* (Feri et al., 1994; Hassler, Steinmetz and Gawlowski, 1988; Hassler, Steinmetz and Pirschel, 1989; Newell, Grady and Sirota, 1989; Perry et al., 1990; Werner et al., 1990). Multimodality monitoring using laser Doppler flowmetry and TCD during cerebral tamponade has shown that positive flow through the basal arteries can be seen after the patient has coned with no net flow through the capillary bed (Figure 13.13; Kirkpatrick et al., 1994a). Such real-time observations concur with the reports using angiographic techniques, showing that the basal cerebral arteries remain patent during early stages of circulatory arrest (Hassler, Steinmetz and Gawlowski, 1986). One explanation for this phenomenon would be the presence of internal cerebrovascular shunts that bypass the parenchymal small vessel networks, reinforcing the concept that initial blood flow obstruction occurs at the level of the capillary.

Although high specificity and sensitivity have been reported using various TCD criteria for brain death (Perry et al., 1990), false positives have been reported, more commonly in children. Consequently, TCD measurements have not been included in the formal testing for brain death. At present TCD can be considered as a useful diagnostic aid in patients who are progressing towards brain tamponade.

### 13.8 Summary

Although measurement of basal vessel FV using TCD has restrictions in terms of quantification and spatial resolution, monitoring of the MCA FV in head-injured patients has produced data that have improved our understanding of cerebral hemodynamic changes following cerebral injury. *The most important contribution has been derived from observing the FV changes with falling CPP and the evolution of the concept that CPP should be maintained above a certain threshold level. That threshold is different between patients, but an ‘average’ value of between 60 and 70 mmHg would...*
Figure 13.12  (a) A graphical display of multiple parameters measured during a 200 ml infusion of mannitol (20%), which was preceded by an identical infusion of normal saline (arrowheads). Mannitol caused a rapid increase in FV and LDF signals, which was associated with a fall in ICP. These changes were not seen after saline. BP remained unchanged throughout the recording period. (b) Mean changes in FV (± s.e. of mean) recorded over approximately 60 minutes during and after a single mannitol infusion from patients with diffuse head injuries (number of infusions = 23). The first point for each recording represents the start of infusion, which was complete at \( t = 0 \) min. In all patients a rise in FV was seen, which decayed soon after completion of infusion. Mean change in FV for all mannitol infusions shown. (\( t = 0 \): time of completion of infusion of mannitol; \( t = 15 \): 15 minutes after completion of mannitol.) (c) The decay of the effect of mannitol on FV after completion of mannitol infusion (time = 0 minutes). The FV has been normalized to a relative baseline of 1 and maximum effect of 2. The fall of FV fits an exponential model with a decay time constant of 34 minutes. ICP = intracranial pressure (mmHg); BP = mean arterial blood pressure (mmHg); FV = right middle cerebral artery flow velocity (cm/s); LDF laser Doppler flux from the right frontal region; AU = arbitrary units. (Source: reproduced from Kirkpatrick et al., 1996, with permission.)
Figure 13.13  Progressive fall in CPP during cerebral coning in a head-injured patient who did not respond to treatment. The progressive failure of microcirculatory flow is seen in the decline in the LDF signal. FV remained positive and later became reverberant. ICP = intracranial pressure (mmHg), CPP = cerebral perfusion pressure (mmHg), FV = right middle cerebral artery flow velocity (cm/s); LDF = laser Doppler flux from the right frontal region; AU = arbitrary units. (Source: reproduced from Kirkpatrick et al., 1994a, with permission.)

**seem appropriate for most individuals.** Other contributions include the facility to discriminate between different causes of raised ICP in real time, allowing an earlier, more targeted hence more appropriate, approach to therapy. Thus TCD can be used to distinguish between raised ICP due to cerebral hypoperfusion, and that due to hyperemia.

Future development of TCD in head injury appears to lie in its incorporation into multimodality monitoring systems, allowing identification of thresholds for
neuronal injury. Dynamic monitoring is also likely to be of considerable use in the evaluation of compounds that aim to assist the injured brain by mechanisms that improve CPP or affect the cerebral vasculature.

13.9 References


REFERENCES