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An Automated Cerebral Blood Flow Analyzer: Concise Communication

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We present an automated cerebral blood-flow (CBF) analyzer that can be used as an intermittent CBF monitor during carotid endarterectomies. Given a 1-min sample of an intracarotid injection of xenon-133, this device will display a CBF value with a range from zero to 200 ml/100 g per min. Results from this CBF analyzer were compared with those from manual computations in 181 separate determinations during 51 surgical procedures. The analyzer is effective, accurate, and reliable.

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The routine use of electroencephalography and cerebral blood-flow measurements during surgery has helped to reduce the risk of endarterectomy at this institution (*1,2*). An automated cerebral blood-flow (CBF) analyzer was developed to permit the determination of CBF without the presence of highly skilled technical personnel familiar with the complexities of these measurements. The initial-slope analysis is ideal for measurements of CBF during surgery (*3,4*).

METHODS

CBF calculation. The principal idea involved in the initial-slope method is that blood flow in the cerebral gray matter dominates the first part of the initial fall period of the clearance curve. Specifically, the first 1–2 min of the clearance curve can be considered as a monoexponential function. The initial-slope equation can be described as:

$$\text{CBF} = 0.87 \times 2.3 \times F_{\text{initial}} \text{ ml/g per min}, \quad (1)$$

where 0.87 is the tissue-to-blood partition coefficient for xenon-133 in gray matter, 2.3 is the factor for converting common to natural logarithms, and F_{initial} is the numerical value of the slope in a semi-log (base 10) recording system.

It must be remembered, however, that these determinations are an approximation and that the lag time of the clearance curve must be taken into account, that is, the time between the actual injection and the beginning of gray-matter washout.

The automated CBF results were checked against those derived manually from the linear strip chart. The latter method used the following formula:

$$\text{CBF } (F_{\text{initial}}) \text{ ml/100 g per min} = \frac{0.87 \times 0.693 \times 60 \times 100}{T_{1/2} \text{ (sec)}} = \frac{3618}{T_{1/2} \text{ sec}}, \quad (2)$$

where 0.87 is the partition coefficient for Xe-133 between blood and brain; $T_{1/2}$ is the time required for the recorded counting rate of the clearance curve to decrease from the maximum to half maximum; and 0.693 is the natural logarithm of 2.

Instrumentation. To meet the needs of a CBF monitor as discussed previously, the device must operate in real time and must be as simple and as reliable as possible, consistent with the functions being performed. Our instrument was designed around hybrid and integrated circuitry to produce modular components so as to minimize failure rate.

The modular components are shown as a block

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diagram in Fig. 1. Figure 2 shows a photograph of the panel.

CBF analysis. After injection of xenon-133 into the carotid artery, a pulse is initiated by the operator to start the timing circuit. The sampling of the logarithmic peak count rate is delayed by 10 sec to compensate for the lag time of the washout curve. This peak count is then held for 1 min by a sample/hold circuit while a differential amplifier subtracts the count rate of the logarithmic curve at the end of 1 min. This value is then multiplied, by a noninverting amplifier, by 20.01 to give the product of the partition coefficient (0.87) and the factor 2.3 for converting common to natural logarithms, and to increase the gain tenfold to drive the digital panel meter. The circuit and associated timing are shown in Fig. 3.

Evaluation. The instrument was tested in the operating room during carotid endarterectomy procedures along with the manually calculated procedure using Eq. 2. This provided a means for simultaneous comparison of the two methods. Fifty-one patients, from whom 181 clearance curves were derived, were used in this evaluation program.

Xenon-133 was monitored by a single thallium-activated sodium iodide detector. The crystal, 1.25 in. in diameter by 0.25 in. thick, was recessed 1 in. behind a tapered lead collimator with an opening widening from 0.875 to 1.125 in. at the surface of the crystal. The detector was placed adjacent to and at right angles to the skull over the parietal boss. Xenon-133 dissolved in saline was injected into the exposed internal carotid artery using a concentration of 200–300 μCi in a volume of 0.2–0.3 ml. Routinely, three measurements were obtained: before, during, and after occlusion. A fourth measurement was obtained if a shunt was used.

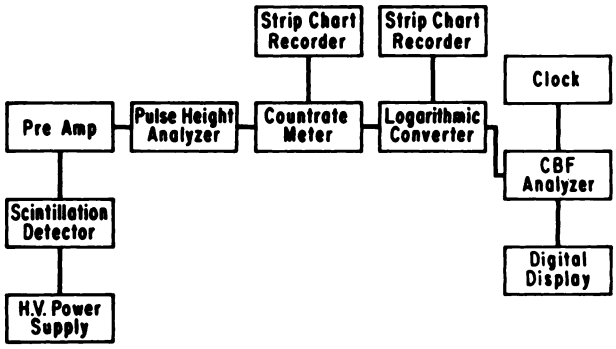

FIG. 1. Block diagram of CBF analyzer.

FIG. 2. Analyzer's panel controls.

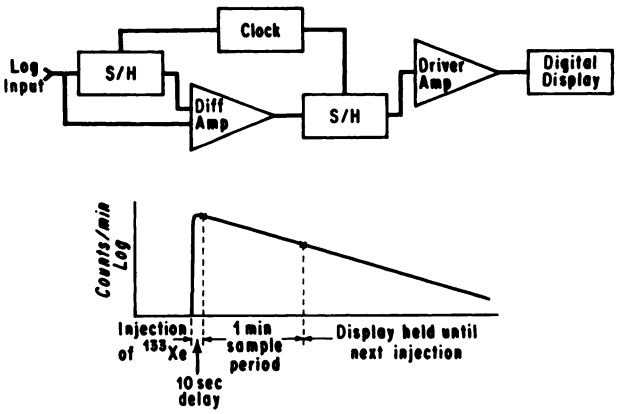

FIG. 3. Block diagram of analyzer circuitry and its associated timing arrangement.

RESULTS

Regional cerebral blood flow computed by the analyzer showed excellent correlation with the manual method of computation. The coefficient of correlation (r) was 0.95, with $p < 0.001$. The correlation of CBF (analyzer) and CBF (manual) is shown in Fig. 4.

The values for CBF were not equivalent, however. Values for CBF (analyzer) were slightly higher than CBF (manual) at the higher-than-normal flow rates. The relationship between CBF (analyzer) and CBF (manual) was more nearly equivalent at moderate and slower clearance rates.

DISCUSSION

During previous carotid endarterectomy procedures at this institution, CBF has been computed manually, using a slide rule and Eq. 2. The value for CBF initial was available to the surgeon within 3 min for flow rates greater than 30 ml/100 g per min. At flow rates below 20 ml/100 g per min, however, more time is required for the manual measure-

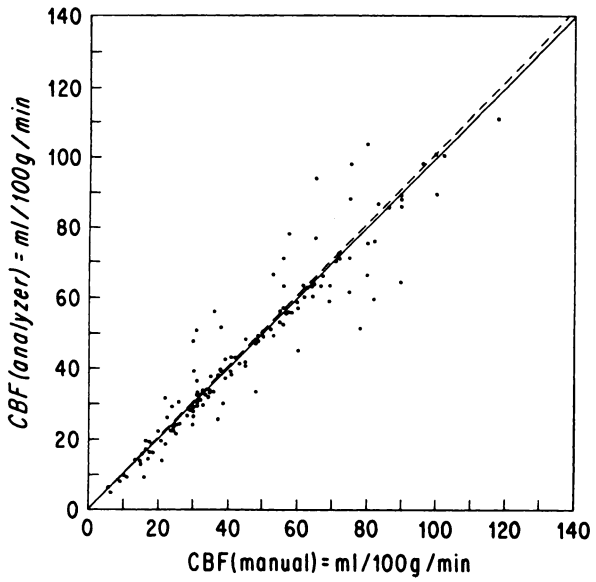

FIG. 4. Correlation of automated CBF with manual CBF in humans, based on 181 measurements. Solid line represents identity and broken line is line of regression.

ment. Furthermore, injections cannot be repeated within 2 min because of the relative contribution of the remaining background activity from the previous measurement, which can cause overestimation of CBF by as much as 10%, depending on the manner in which the background is treated in the calculation (*5*).

Ideally, correction of remaining background activity requires the extrapolation of the tail part of the previous clearance curve. This method, however, requires an on-line computer system and prolongs recording of the clearance curves by as long as 30 min. This is impractical during surgery because the delay imposed between successive measurements increases the risks of anesthesia and surgery for the patient. It was our established custom to wait 5–10 min between successive curves when using manual methods of flow computation. The waiting period varied and depended on the flow, but it was necessary in order to minimize the contribution of background activity from the previous injection, which was substantial in low-flow situations. The failure to wait this required time introduced a significant error in the succeeding measurement by altering the slope of the washout curve, particularly in that portion of the curve after the initial 2 min.

When the measurement is done with the CBF analyzer, flow rate is calculated (Eq. 1) from the slope of the first minute of the clearance curve, excluding the curve's lag portion. Thus the measurement of the slope in 1 min minimizes the error of measurement from residual background activity. With this technique, the minimum time interval between injections was 90 sec.

The analyzer was designed to be operated with a minimum of technical knowledge; all functional controls are preset. This extends the possible use of CBF measurements to institutions lacking biomedical engineering support.

There was excellent correspondence between the electroencephalogram and the levels of CBF considered to be critical. The critical CBF, defined as that required to maintain basic cerebral metabolism and normal electrical activity, has been found to be 15–17 ml/100 g per min at a Pa_{CO_2} of 40 torr (*1,6–8*). This flow level represents the minimum required to prevent infarction, but it does not provide for normal cerebral function. This is related, in part, to the regional requirements of the brain for blood, and varies according to functional demands in patients with normal autoregulation. The selection of the parietal area for CBF measurement during surgery is important as this is the watershed area; accordingly it is most likely to have a low flow with carotid occlusion.

The use of a single probe rather than several is of considerable and practical importance because it enables institutions having appropriate support in the field of nuclear medicine to make these types of measurement routinely without procuring items of equipment that are prohibitively expensive, cumbersome, and unlikely to be tolerated in the operating room by an average surgical team. The very close correlation between the studies using a single probe and those using multiple probes is quite striking (*1,9,10*). This correlation and the simultaneous EEGs performed in both studies suggests that (at least for studies in which ischemia is produced by occlusion of a single major vessel in the neck) the reduction in hemispheric blood flow is more uniform, with less regional variation, than that found in cases where ischemia results from occlusion of an intracranial vessel (*9*). Analysis of the cases reported by Boysen substantiates this view. Furthermore, in over 500 cases operated on to date, monitored by simultaneous EEG and xenon CBF measurements, we have never had, during carotid occlusion, an electroencephalogram change that was not reflected by an appropriate blood-flow change—except in three cases in which the EEG changed because of embolization in a small intracranial vessel. In this instance, the xenon CBF measurements failed to detect the focal area of ischemia because of problems related to "look-through" and Compton scatter (artifacts of measurements that cannot be totally excluded even with a multiple-probe system).

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