Continuous Measurement of Regional Cerebral Blood Flow Using Krypton-81m

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SUMMARY We have developed a new method for taking continuous measurements of rCBF by means of continuous infusion of $^{81m}$Kr. Using this method, it is possible to follow the sequential changes in blood flow of various brain regions continuously. The method makes it possible to observe the sequential changes in CBF following drug administration, motor activation and various kinds of stimulation, and, furthermore, to observe the $CO_2$ reactivity and autoregulation of cerebral vessels. It will undoubtedly prove useful in the investigation of various pathological states.

Method

Kr-81m solution was produced by pathing 5% glucose solution through a 10mCi Rb-Kr generator (Japan Mediphysics Co). The solution, with constant concentration, was infused continuously to the internal carotid artery (ICA) at a constant rate of 3ml/min through a catheter inserted into the ICA using a perfusion pump (Truth A-II). Under these conditions, lateral image of the head and neck were obtained by a $\gamma$-camera (Toshiba GCA 301). The obtained images were fed online into a data processor (Toshiba GNS 80A). Sampling time was 30 seconds a frame and 60 frames of the sequential data obtained every 30 seconds were collected in 30 minutes.

Theoretical Consideration

In the intracarotid Kr-81m infusion method, regional radioactivity of the brain can be obtained from the following equation:

$$Ciq \propto \frac{fi}{(\mu + vi/\lambda)i}$$

where, Ciq is the regional radioactivity obtained from the surface of the skull, fi is the regional CBF, $\mu$ is the decay constant, vi is the volume of brain tissue perfused by radioisotope, $\lambda$ is the partition coefficient between blood and tissue.

Since the half-life of $^{81m}$Kr is as short as 13 seconds, the regional radioactivity (Ciq) is roughly proportional to rCBF (fi). Consequently, the equilibrium image of the brain infused with $^{81m}$Kr is said to express this regional distribution of CBF. However, in the case of...
observations on the sequential changes in rCBF, it is necessary that the concentration of $^{81m}$Kr in the blood perfused to the brain through the ICA is constant, in order that equation 1 can be applied. Since using this method a constant volume of $^{81m}$Kr is infused per unit of time, changes in radioisotope (RI) concentration in the blood perfused to the brain correlate with changes in the blood flow through the ICA. Consequently, when sequential changes in CBF are measured under these conditions, it is necessary to express the relative rCBF as the proportion of regional radioactivity to the $^{81m}$Kr concentration of the blood perfusing the brain. That is,

$$C_{\text{ieq}}/C_{\text{RI}} \propto \frac{fi}{(\mu + fi/v_i \cdot \lambda)}$$

where, $C_{\text{RI}}$ is the concentration of $^{81m}$Kr in the blood perfused to the brain.

In order to find $C_{\text{RI}}$, we have utilized the radioactivity (count rate) obtained simultaneously from the region of interest (fig. 1, Region of Interest 7) set above ICA and used it as an index of the RI concentration of the blood perfused to the brain. That is, the value obtained by dividing the count rate in each frame (30 seconds) from each area of interest above the brain (fig. 1, Region of Interest 1–6) by the count rate obtained in each frame from the cervical ICA (fig. 1, Region of Interest 7) is taken as the relative value and such relative values are continuously recorded.

Using this method and normal subjects, CO$_2$ inhalations were undertaken. Marked increases in CBF were found and the effectiveness of the method confirmed. Finally, the method was used in clinical cases.

Results and Clinical Uses

1. CO$_2$ Reactivity in Normal Subjects

Almost no changes in count rate ($C_{\text{ieq}}$) obtained every 30 seconds from each area (fig. 1, Region of Interest 1–6) were seen following inhalation of 10% CO$_2$ in air (fig. 2). In contrast, there was a definite decrease in the count rate obtained from the region above the cervical ICA due to inhalation of CO$_2$ (fig. 1, Region of Interest 7, fig. 3 bottom line). When inhala-
Sequential changes in the value obtained from the count rate of the individual ROI of the brain divided by the count rate of the cervical internal carotid artery. These sequential changes indicates changes in cerebral blood flow following CO₂ inhalation.

Sequential changes in the values obtained by dividing the count rate of each ROI of the brain at each time interval by the count rate obtained at the region above the cervical ICA were also observed (fig. 4). Following CO₂ inhalation, a slow increase was seen for about 2 minutes, at which time a plateau was reached. Cessation of inhalation caused a decrease until the pre-inhalation level was reached after 1 minute. These changes are thought to accurately reflect the sequential changes in CBF due to CO₂ inhalation.

2. Use in Clinical Cases

Investigation of autoregulation using this method was done during the period of marked clinical disautoregulation in a case of ruptured cerebral aneurysm and during the subsequent period when the patient was clinically without symptoms.

The patient was a 33 year old male with aneurysm of the anterior communicating artery. He experienced sudden headache on April 14, 1980 followed by loss of consciousness for about 10 minutes. Radical surgery was performed on the aneurysm on the 3rd day from onset, but on the 7th day blood pressure fell and right hemiparesis appeared. Symptoms disappeared, however, when blood pressure rose to 160/110 mmHg and it was apparent from clinical signs that there was a disturbance in autoregulation. At this time, an investigation of the autoregulation was carried out (fig. 6A). When blood pressure rose due to drip infusion of Hypertensin (Ciba®), the rCBF of the left cerebral hemisphere rose (fig. 5) at all areas together with rises in blood pressure from an average pressure of 90 mmHg to 120 mmHg. This finding indicated that there was a loss of autoregulation in the entire left cerebral hemisphere.

On the 16th day from onset, a fall in blood pressure to 120/80 mmHg resulted in disappearance of symptoms and autoregulation was again tested on the 30th day (fig. 6B). Although average blood pressure rose from 100 mmHg to 140 mmHg, rCBF showed almost no changes, indicating the recovery of autoregulation.

Discussion

In order to measure the sequential changes in cerebral blood flow continuously using the intracarotid ⁸¹mKr infusion method, we devised a new technique using the radiation from the cervical carotid artery as an index of the concentration of the radioisotope in the blood perfused to the brain. Under continuous intra-
carotid injection of $^{81m}$Kr, the radioactivity obtained from the surface of the skull is proportional to the cerebral blood flow. However, since the method depends upon the infusion of a given volume of radioisotope per unit of time into the internal carotid artery, changes in blood flow through the internal carotid artery result in changes in the concentration of radioisotope perfused to the brain. Under such conditions, the radioactivity obtained from the surface of the skull does not indicate the changes in blood flow. In such a case, the value obtained from the radioactivity (count rate) in the region of interest of the brain divided by the concentration of radioisotope in the blood perfused to the brain indicates the changes in cerebral blood flow. Our attention was drawn to the fact that radioactivity measured from a constant area of the cervical internal carotid artery per unit of time is an indicator of the blood concentration of radioisotope flowing in the internal carotid artery. The results of an investigation of CO$_2$ reactivity and autoregulation using this method are thought to accurately reflect the normal vascular responses and changes in clinical symptoms.

In the current study, we have assumed that the relative CBF per unit of time is equal to the ratio of the count rate of a cerebral region obtained every 30 seconds (in each frame) and the count rate at the cervical ICA. In fact, however, a certain amount of time is required for the isotope to become equally distributed in the brain from the time of injection, leading inevitably to a certain error in our final values. The amount of time until equal distribution in the brain is perhaps 30–60 seconds, so that, under the current conditions for measurement with a sampling time of 30 seconds, this time factor is not thought to constitute a major problem.

It should also be noted that we used the radioactivity measured per unit of time in the cervical ICA as an index of $^{81m}$Kr concentration in the blood flowing through the ICA. In order for this assumption to be true, it is necessary that the volume of blood in the ICA should be constant. However, when there are changes in the blood flow in the ICA, the diameter of the lumen of the ICA changes and this is thought to result in changes in the blood volume at the region being measured. Nonetheless, in comparison with the changes in blood flow in the ICA, the changes in the lumen of the ICA are thought to be extremely small, so that the influence of this factor can be ignored.

As seen from the above, it appears that there is still a need for technical improvements in this method for measuring CBF, but currently it does allow for continuous recording of dynamic changes in rCBF which has been impossible with previous methods. From an investigation of the CO$_2$ reactivity and the autoregulation of cerebral vessels, it should also be possible to

FIGURE 6. rCBF changes following change of blood pressure by drip infusion of Hypertensin CIBA® (MBP: mean systemic blood pressure). A: 10 days after the onset: rCBF correlated with the change of blood pressure. B: 30 days after the onset: rCBF showed no change.
measure local changes in CBF following drug administration or cerebral activation due to motor activity, visual or auditory stimulation. Recent developments in emission CT scanning have made it possible to obtain 3-dimensional measurements of CBF which have also been used in conjunction with the single photon emitter 81mKr. Our technique described above should also be applicable to 3-dimensional studies using the emission CT scanner by making measurements of radioactivity at the cervical ICA. We believe that our method for making sequential measurements of CBF will find many uses in the investigation of various pathological conditions.

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