

operator intervention required at this time is in the verification of the accuracy of the mask. The method will fail in the event of gross anatomic asymmetries, however these problems will be easily detectable.

#### No. 442

GENERATOR PRODUCED I-122 LABELED AMINES AND DIAMINES FOR BRAIN BLOOD FLOW MEASUREMENTS IN NEUROLOGIC DISORDERS. CA Mathis, TF Budinger, T Sargent III, AT Shulgin, and HF Kung\*. Donner Lab, U. of Calif., Berkeley, CA 94720 and \*VA Medical Center, Buffalo, NY

In response to a need for an extracted brain blood flow tracer for positron tomography, we have developed from our original iodoamphetamine an I-122 radiopharmaceutical produced from a 20h Xe-122 generator and have demonstrated its application in animals and humans. The I-122 (t<sub>1/2</sub> 3.6m) is collected in the reaction vessel by a 10 min ingrowth from the Xe-122. The radiopharmaceutical, 2,4-dimethoxy-N,N-dimethyl-5-[I-122]iodophenylisopropylamine (5-[I-122]-2,4-DNNA), is synthesized using I-122 and chloramine-T, purified and sterilized for injection in 3 min. Synthesis can be repeated every 20-30 min. The diamine HIPDM was also labeled with I-122 by an exchange reaction for comparison. Using the Donner 280 crystal tomograph system, anesthetized dogs showed rapid uptake of the activity in the brain using 5-[I-122]-2,4-DNNA and I-122 HIPDM. The ratio of activity in the brain to surrounding tissue was 6:1 and the distribution was the same as that from 18-FDG injected 30 min later. Patients with ischemic brain disease were injected with I-122 HIPDM and the images showed blood flow deficits in the regions of low FDG uptake which also corresponded to anatomical sites anticipated by clinical signs. PET studies of flow and metabolism are being applied to patients in whom recurrence of brain tumor needs to be differentiated from radiation necrosis as well as in stroke and Alzheimer's disease patients.

#### No. 443

3-FLUORO-DEOXYGLUCOSE FOR THE ASSESSMENT OF CEREBRAL PERFUSION AND GLUCOSE TRANSPORT - INDICATIONS FOR EXTRACRANIAL-INTRACRANIAL ARTERIAL BYPASS AND FOLLOWUP STUDIES. H.M. Mehdorn, K. Vyska, H.-J. Machulla, E.J. Knust. University of Essen Medical Center, Essen, Herzzentrum NRW, Bad Oeynhausen, FRG

3-Fluor-Deoxyglucose (3FDG) is a glucose-analogue which is transported across the blood-brain-barrier by the same carrier as glucose but is only phosphorylated to a minor part. By a newly developed model, it became possible to estimate both cerebral perfusion and glucose transport in a single examination, determining the Michaelis-Menten-constant  $K_m$  and the maximal velocity  $v_m$ . Normal values were determined as follows: gray matter perfusion 88±8 ml/100g min;  $v_m$  was 2.46  $\mu$ mol/g min;  $K_m$  was 6.42  $\mu$ mol/g.

This method was applied successfully in a series of 15 patients with cerebral ischemia to select suitable candidates for extracranial-intracranial (EC-IC) arterial bypass surgery and to follow them up to 15 months postop.

In patients with minor strokes and transient ischemic attacks (TIA), areas which appeared normal in conventional CT presented with reduced perfusion values (down to 67 ml/100 g min) and either normal or reduced  $v_m$  (down to 0.8  $\mu$ mol/g min). These patients were thought optimal candidates for EC-IC bypass in order to improve the misery perfusion state. Clinical followup examination showed improvement of a neurologic deficit and/or no further TIAs. This correlated well with improvement of  $v_m$  and cerebral perfusion to normal values. On the other hand, areas of infarction on conventional CT scan showed no improvement of  $v_m$  although some increase of cerebral perfusion was seen indicating that a useless increase of flow had occurred.

#### No. 444

IN VIVO EVALUATION OF POTENTIAL Tc-99m BRAIN PERFUSION AGENTS USING BRAIN UPTAKE INDEX DETERMINATION AND BIODISTRIBUTION. A.J. Rajeckas, A.D. Watson, V.

Subramanyam, S.J. Williams, B.Q. Belonga, E.I. DuPont de Nemours, NEN Medical Products, Billerica, MA.

In order to evaluate the pharmacological properties of various Tc-99m complexes as potential brain perfusion agents, we have employed both biodistribution techniques as well as a modified Oldendorf procedure for the determination of the brain uptake index (BUI).

A typical BUI determination involves the coinjection of 1 microcurie each of I-125 iodoantipyrine and the Tc-99m complex into the left carotid artery of a pentobarbital anesthetized rat. The animal is sacrificed at 10 seconds; the right and left hemispheres of the brain are removed and counted for each isotope in a gamma well counter. Biodistribution studies are performed using tail-vein injections in unanesthetized rats.

In the evaluation of a series of Tc-99m N<sub>2</sub>S<sub>2</sub> (diamine dithiol) complexes, we have observed that compounds with a low BUI (less than 50) also have a low brain concentration (less than 1% ID) at 30 seconds post injection. However, there are examples of Tc-99m complexes with high BUI values (80-90), which show a low concentration in the brain at 30 seconds post injection. These observations imply that each technique provides different information which may be valuable in assessing the pharmacological properties of potential brain agents. Correlation of BUI with the lipophilicity of these complexes as measured by partition coefficient and HPLC retention times on C18 reverse phase media suggest that lipophilicity is a necessary, but not sufficient, characteristic for high brain uptake of a Tc-99m complex.

#### No. 445

REGIONAL CEREBRAL BLOOD FLOW ABNORMALITIES IN ALZHEIMER'S DISEASE. K. Rezaei, H. Damasio, N. Graff-Radford, P. Eslinger, P. Kirchner. University of Iowa, Iowa City, IA.

In 37 patients (ages 58-81) with senile dementia of Alzheimer type (SDAT), regional cerebral blood flow (rCBF) was studied utilizing a dedicated SPECT system (Tomomatic-64) that produces rCBF images from 4-minute clearance of Xenon-133 in the brain. We have modified the device to acquire 5 contiguous tomographic slices simultaneously.

A consistent pattern of diminished blood flow was seen in 33 patients in the posterior-temporal and lower-parietal brain regions. Computer programs were developed to quantitate the size of the affected brain tissue in the posterolateral brain areas (confined to the posterior 40% and the lateral 25% of the major and minor brain axes respectively). We have previously reported normal rCBF in 25 volunteers to be greater than 45 ml/min/100g with less than 10% regional variation. Hence, an area was considered abnormal if rCBF measured less than 40 ml/min/100g or was less than 70% of the mean rCBF value in the anterior temporal-frontal regions. The mean size of low rCBF regions in the 37 SDAT patients was 30.3% of the analyzed areas, while the mean measurement in a group of 7 age-matched normals was 2.3%. In 4 SDAT patients, findings were indistinguishable from those in controls. In 201 rCBF studies on non-dementia patients, a similar pattern of reduced rCBF was found in only 7: 4 of these patients had vertebral-basilar insufficiency, 2 had thalamic infarcts, and 1 had anterior circulation TIA.

The abnormal rCBF findings in SDAT patients suggest decreased neuronal activity in posterior association cortices related to complex visual and auditory processing. The test should prove useful in diagnosis of Alzheimer's Disease.

#### No. 446

Xe-133 rCBF MEASUREMENT REPRODUCIBILITY AND NORMAL LIMITS OF ASYMMETRY. E.B. Silberstein, W. Carney, E.D. Means, G.C. Rauf, V. Madden, R. Noll. Veterans Administration Medical Center, Cincinnati, OH.

New software for determination of regional cerebral blood flow (rCBF) has been added to equipment using Xe-133 inhalation and 32 p-m tubes in a helmet-like configuration (NOVO Cerebrograph 32c). We examined the reproducibility of rCBF measurements and the degree of asymmetry acceptable as normal. The 2 parameters studied were initial slope index (ISI) and CBF15, both heavily weighted toward the fast clearing compartment (largely grey matter)