protein in patients with dementia has also been measured. Disturbances of cerebral blood flow and metabolic activity have been observed which can be in part non specific and the consequence of neuronal cell loss.

PET studies about focal epileptic lesions have been reported. It seems that during an ictus glucose metabolism is increased in the affected area, whereas, inter-ictally a zone of hypometabolism is present.

Although the task appears much more difficult PET has been used to map neuronal dysfunction in mental disease, paticularly in schizophrenia. ^{11}C-Methionine and ^{18}F-FDG have been used by several groups. Labeled ligands which bind specifically to receptors will probably bring new information in that field.

FDG studies on Huntington's chorea and Parkinson's disease have also been reported. Recentlyusing L-Dopa labeled with ^{18}F, a reduced uptake of the tracer has been shown in the striatum. L-Dopa study could be coupled to ligands for the dopamine receptor such as ^{11}C-Methylspiperone, ^{76}Br-Bromospiperone or ^{11}C-Raclopride. For the first time a loss of striatal dopamine receptors in patients with progressive supranuclear palsy has been demonstrated in vivo by PET using ^{76}Br-Bromospiperone.

The potential of PET is thus obvious; the present results which are already spectacular are however preliminary. Emphasis is now put on receptor studies and a large number of specific ligands will soon be available. For brain studies one can quote ligands for dopamine, benzodiazepine, serotonine, acethylcholine and opiate receptors. PET studies are not only confined to brain and heart but can also be used to investigate other organs such as pancreas, lungs or kidneys. Thus, even if PET procedures cannot be installed on a large scale in the future, this method produces unique results which cannot be obtained by an other technique including NMR imaging and spectroscopy.

II

IMAGING OF CUTANEOUS T-CELL LYMPHOMAS WITH MONOCLONAL ANTIBODIES.

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"Radioimmunodetection" is an in vivo diagnostic approach using anti-tumor antibodies to carry radioactivity to tumor cells. Several authors have used I-131 polyclonal antibodies directed against tumor products such as CEA and alpha-fetoprotein for clinical studies. In general, though these procedures have detected some primary or metastatic tumor sites, such scans have not been sufficiently sensitive or specific for routine applications. Hybridoma-derived monoclonal antibodies (MoAb) offer potential advantages over the polyclonal reagents including greater purity, specificity and lack of variability between lots. In contrast to I-131 radiolabeled antibodies, In-111 may have higher stability in vivo with improved tumor concentration.

T101 is a murine MoAb IgG2a (Hybritech, Inc., San Diego, CA) that recognizes a 65,000 dalton glycoprotein (T65) on most T-cell malignancies, B-cell chronic lymphocytic leukemia (CLL), and in less abundance on circulating mature normal T-cell but not on most normal B-cells, granulocytes, monocytes or platelets. The T101 was purified from hybridoma ascites of BALB/c mice by precipitation with 18% Na sulfate. A modification of the Krejcarek method was utilized to conjugate approximately two diethylene-triaminepentaacetic acid (DTPA) moieties per molecule of antibody. The antibody was received in kit form (Hybritech, Inc., San Diego, CA) consisting of 1mg DTPA-conjugated T101 MoAb in 1% human serum albumin (HSA). Labeling was performed by incubating approximately 5mCi I-111 with 1mg of DTPA conjugated T101. Excess DTPA was then added to scavenge any free In-111. Ninety-five percent of the I-111 was incorporated onto the T101. The immunoreactivity of this product was preserved with a mean of 88% as determined by a cell binding assay.

Dose escalation studies were performed by co-injecting 0 mg, 9 mg, or 49 mg of carrier unconjugated T101 with 1 mg of In-111-T101 for a final concentration of approximately 1, 10 and 50 mg respectively. T101 was infused intravenously over 2 hours at 1 and 10 mg , and over 6 to 9 hours for the 50 mg level to minimize side effects. Vital signs were monitored and serial blood and plasma samples were obtained.

Eleven patients were studied following injection of 1 mg to 50 mg of T101. In all patients, In-111-T101 concentrated in pathologically or clinically involved nodes including several previously unsuspected nodal regions. Focal uptake was seen in skin tumors and heavily infiltrated erythroderma but not in skin plaques. Patients receiving $\geq$ 10 mg antibody had itching, urticaria and chills. The concentration of radioisotope in diseased nodes ranged from 0.01 to 0.03% of injected dose per gram. The specificity of

uptake was documented by lack of tumor visualization with $^{111}I\,Cl_3$ or 9.2.27 (anti-melanoma) monoclonal antibody.

The blood clearance of 1 mg of ^{111}In-T101 was very rapid with less than 10% retained in blood at 2 hours post injection. The 10 mg and 50 mg dose of T101 demonstrated more prolonged blood pool circulation of the ^{111}In-T101. All nodal lesions were well seen at all dose levels. At all dose levels whole body retention of ^{111}In-T101 was prolonged (T 1/2 > 7d).

Modulation of the antigen from skin, lymph nodes and circulating cells was seen. Previous studies by Schroff et al have shown internalization of the T101 once it binds to the T65 antigen. Consistent with kinetics studies of Sezary cells performed by Bunn, it is felt that these cells targeted with ^{111}In-T101 are capable of traffiking to involved lymph nodes and skin tumors.

In three patients the T101 was labeled with I-131 via the chloramine T method (mean - 1.2 mg, 2 mCi). The quality control showed that the injected antibody had an immunoreactivity of 75%. Antibody administration, biodistribution measurements and scanning was performed in a similar fashion to that of the ^{111}In-T101 antibody studies described previously.

Nodal uptake was minimally seen in 1 patient and absent in 2 patients receiving ^{131}I-T101. One of these latter patients received ^{111}In-T101 3 days after ^{131}I-T101 and showed excellent uptake involved nodes and skin.

The blood clearance of ^{131}I-T101 was rapid. The whole body clearance was significantly shorter than that of ^{111}In-T101 (<2 days). Although initially there was prominent uptake in the liver, and spleen as well as mild bone marrow uptake, this cleared quickly, in contrast to ^{111}In- T101, which had prolonged retention in those organs. These findings indicated rapid dehalogenation with excretion of the I-131 label.

No side effects were seen in patients receiving 1 mg of T101 but in all patients receiving ≥ 10 mg self limited chills and urticaria was observed.

These studies suggest that imaging with ^{111}In-T101 may be of value in identifying sites of nodal involvement in patients with cutaneous T-cell lymphomas, and also demonstrate major differences in biodistribution with ^{131}I-T101. The accumulation in involved lymph nodes revealed consistent targeting of radiolabeled antibody at levels 10 to 100 times higher than previously reported for radioimmunodetection.