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19. ABSTRACT (Continue on reverse if necessary and identify by block number) Two geriatric male rhesus monkeys were used for the radioisotope imaging in this research. Discussion of the radionuclide, materials and method used to accomplish the neurologic examination and the results obtained, both during the procedure and confirmation of the of the results by necropsies were accompanied by color photos of scan images. Results were that the nuclear images provided accurate images of intracranial neoplasia. (SDW)			
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Radioisotope Imaging of Brain Tumors in Two Rhesus Monkeys

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Nuclear imaging involves the systemic administration of a radionuclide (radioisotope) to a patient after which a picture or image is generated by recording relative quantities of radiation emitted from regions of interest in the patient (1-6). The picture is formed from the digital radioactive counts acquired during the procedure (4). This information can be recorded by a computer so that images and digital information can be recreated for later analysis. By integrating the intensity of regions of the screen images, objective measurement of differences in radioactivity level can be made.

The most commonly utilized radionuclide is Technetium - 99m (^{99m}Tc), which emits gamma rays at 140 keV and has a 6 hour physical half life (1,4). The radionuclide is usually bound to another pharmaceutical chosen for its biologic behavior to result in localization to a specific region of interest in the body (1).

Nuclear imaging has been employed in veterinary medicine for brain, bone, thyroid, hepatic, lung and cardiac studies (1,7-11). We described two cases of intracranial neoplasia in rhesus monkeys which were characterized with the aid of ^{99m}Tc brain scans.

Two wild-caught male rhesus monkeys, 19 and 21 years of age, were examined for evaluation of apparent blindness, hemiparesis and mental depression. The monkeys were housed individually in covered outdoor cages with thermostatically controlled gas heating during the winter. At 4 years of age both monkeys had been exposed to single, total body doses of ionizing radiation. Monkey #1 received 400 Rad of 55 MEV protons, while monkey #2 received 225 Rad of 2.3 GEV protons. Subsequent to irradiation the monkeys were not used in any other studies. Triannual physical examinations, including complete blood chemistry profiles and cell counts, were performed during the observation period.

The monkeys underwent extensive neurologic examination revealing unilateral blindness, resting and positional nystagmus which varied in direction, proprioceptive deficits, various stages of motor weakness and alteration in normal behavioral status. All clinical signs had a gradual onset. These symptoms were consistent with

a diagnosis of an intracranial space occupying mass. Results of hemograms and serum biochemical profiles for both monkeys were within normal limits. Cerebrospinal fluid analysis of monkey #2 revealed a moderate elevation of protein content to 86 mg/dl. Cerebrospinal fluid analysis for monkey #1 was not done.

Each monkey was anesthetized with ketamine HCl (12 mg/kg IM) and diazepam (2.5 mg IV). An indwelling catheter was placed in the cephalic vein and anesthesia was maintained with repeated doses of both agents. After positioning the monkey so that the base of the skull was centered over the grid of the gamma scintillation counter,¹ a 5 millicurie dose of technetium 99m-DTPA (diethylenetriamine penta-acetic acid) was injected intravenously. A dynamic flow study of the carotid arteries and cerebral hemispheres was performed coincident with injection and was followed immediately by the initial brain scan series. A series consisted of four studies or views of the head, including both lateral positions, a posterior view, and a vertex (parietal) view. Each study was defined by a total of 500,000 counts of gamma radiation from the technetium. The digitized information was recorded on an image processing computer² using commercial software.³ A delayed series was accomplished 2 hours later to determine varied uptake of radionuclide.

Image profiles and time activity curve analyses were performed on each study. An image profile is the graphic representation of radioactivity integrated from a linear plane, the boundaries of which are arbitrarily determined by the computer operator. The computer plots the curve based on the gamma radiation received from this specific region of the image. Regions may be varied at the discretion of the computer operator and multiple profiles produced.

Plotting of a time activity curve is usually done to make comparisons of bilateral anatomic structures. The first step is to identify specific bilateral regions of interest (cursor defined rectangles) on the screen image. Typical regions of interest are the carotid arteries, middle cerebral arteries, and parts or all of the cerebral hemispheres. The computer then graphically illustrates the recording of radiation counts from the entirety of each region over time. Both techniques allow quantification of radioactivity and reduce subjectivity and possibility of error when simply looking at the screen image.

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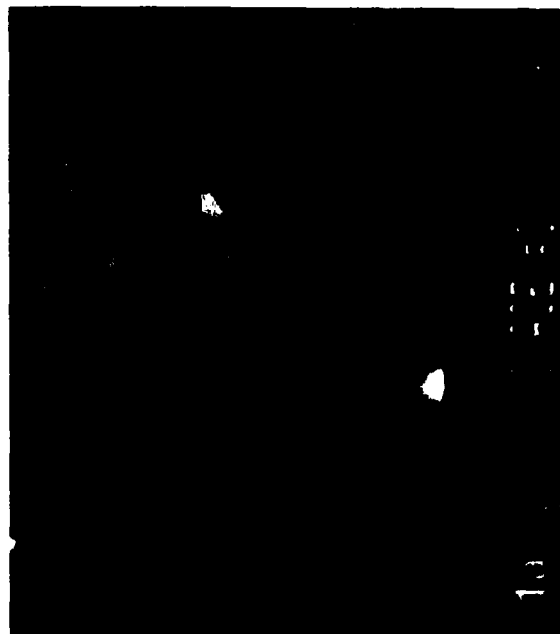


Figure 1a and 1b Vertex and posterior views of monkey #1 showing a region of increased radionuclide activity (arrows) at 2 hours post-administration.

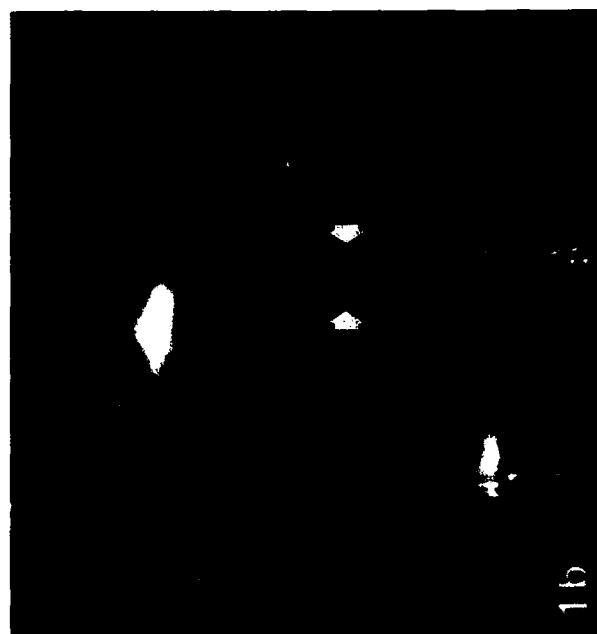


Figure 2 Computer-plotted image profile of monkey #1. The area between the horizontal cursor lines is plotted on the graph, indicating greater radionuclide activity on the right of the midline.



Figure 3 Time activity curve analysis of monkey #1. The radioactivity levels of the cerebral hemispheres are plotted against each other, indicating higher counts in the right hemisphere.



Figure 4 Anterior-posterior view of a transverse section of the brain of monkey #1. The glioblastoma multiforme in the right temporal cortex (arrows) is cavitated and compresses the left ventricle.

In both monkeys, the studies revealed focal regions of increased radioactivity correlating with accumulation of radionuclide. The scan of monkey #1 revealed a focal spherical mass in the region of the right cerebral cortex (Figure 1). The scan of monkey #2 indicated a linear shaped mass at the base of the skull extending from the region of the optic chiasm craniad to the right orbit. Image profiles (Figure 2) and time activity curve analysis (Figure 3) of the scans confirmed an increase in radioactivity in the right hemisphere of the brain of both monkeys.

The monkeys were euthanatized and complete necropsies performed. Necropsy of monkey #1 revealed a 2 x 3 x 3.5 cm. rough, oval, soft, friable light-brown mass involving a majority of the temporal lobe and a portion of the right cerebral hemisphere (Figure 4). The mass protruded 1-2 mm above the surface of the right occipital cortex and extended medially along the internal capsule. The mass compressed the surrounding neuropil and the right lateral ventricle, as well as the left side of the brain. There were multiple, variably-sized areas of cavitation, necrosis and hemorrhage within the mass. The neoplasm was diagnosed histologically as a glioblastoma multiforme. Necropsy of monkey #2 revealed a soft, granular, light-brown mass tightly adherent to the skull at the base of the brain. It incorporated or replaced adjacent meninges and cranial nerves, the optic chiasm and pituitary gland. The mass extended anterior to the right orbit, incorporating the right optic nerve and the extrinsic muscles of the right eye. Posteriorly, the mass extended along the tentorium cerebelli, compressing the cerebrum and cerebellum. The mass was diagnosed histologically as a malignant meningioma.

A brain scan is performed by placing a scintigraphic counter, called a gamma camera, next to the head following radionuclide injection. Information from the

counter is computerized and recorded so visual images are created. Regions where radionuclide has accumulated, commonly called "hot spots", will stand out on the image against the normal background.¹

The isotope used in this study, ^{99m}Tc, is usually bound to an agent which concentrates in the area of diagnostic interest. The principal by which a brain scan functions is the localization of radionuclide in an area of abnormal circulation (5,12). Defects in the blood-brain-barrier, developing vessels in tumors, increased protein binding of some tumors, and other mechanisms allow radionuclide to collect in extracellular fluid (12). Radionuclide in the general circulation undergoes biologic elimination in addition to physical decay. Its initial half-life is about 1.5 hours and subsequent half-times are about 3.5 hours. For the trapped radionuclide, however, the isotope is susceptible only to physical decay, hence gradually increases in intensity and becomes the hot spot. This is a reflection of physiologic rather than anatomic defects as could be seen with tomographic scanning (13).

Technetium 99m pertechnetate has been used extensively for brain imaging in the past (5,12). However, it has the disadvantage of accumulating in the choroid plexus, thus complicating the interpretation of this region (5). In humans, this artifact is eliminated by use of Technetium 99m - DTPA, (3,13) and similar results were achieved in the rhesus monkeys of this study.

Dynamic studies provide angiographic information concerning blood flow to specific regions of the head (3). In Monkey #1 this provided specific evidence of asymmetry between the cerebral hemispheres (Figure 4). Having the ability to quantify radiation levels strengthens the diagnostic capability of the study. Delayed imaging will provide improved visualization of tumors in a majority of cases (4). This allows for greater differential radioactivity between the low background level and accumulation of radionuclide within the tumor (3,4).

Nuclear brain scans are a sensitive technique for screening of brain tumors in both animals and humans (1,2,6,8,13) and have been described as the most practical of nuclear scan procedures for use in veterinary medicine (1). In these two rhesus monkeys, nuclear scans provided accurate images of intracranial neoplasia.

Acknowledgements

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Footnotes

¹Pho-Gamma V Scintillation Camera, Siemens Medical Systems, Inc., Grand Prairie, TX.

²MDS A² Computer System, General Electric Medical Systems Group, San Antonio, TX.

³Cardiovascular Analysis Program Version 2.0, General Electric Medical Systems Group, San Antonio, TX.

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