Technetium-99m Glucoheptonate as a Brain-Scanning Agent

The evolution of brain scanning has seen a number of advancements in both radiopharmaceuticals and instrumentation. Mercury-203 or 197-labeled-chlormerodrin provided a significant increase in sensitivity over I-131-labeled serum albumin; however, after the introduction of Tc-99m by Harper et al (*1*) the use of the mercury compounds decreased. Witcofsky, in a comprehensive study of brain scanning using TcO_4^- (*2*), found an 81.5% sensitivity rate for proven neoplasms of the central nervous system. This study was performed in the mid-1960's and relied upon instrumentation in use at that time. Technetium-99m diethylenetriaminepenta-acetic acid (Tc-DTPA) has been advocated as a superior brain scanning agent when compared with TcO_4^- (*3*), and Waxman et al have demonstrated the advantages of Tc-99m glucohepeonate (TcGH) over TcO_4^- as a brain scanning agent in both tumor and infarction (*4*). Based upon previous reports of glucoheptonate accumulation in acutely infarcted myocardium, Rollo et al postulated that the improved detection of lesions was due to a combination of increased binding to abnormal tissue and a rapid blood clearance of the agent (*5*).

In a comprehensive paper comparing TcGH to TcO_4^- and TcDTPA as effective brain scanning agents, Rollo et al concluded that TcGH was the radionuclide of choice for the detection of central nervous system abnormalities (*6*). The article appearing in this issue of the *Journal* by Leveille et al, entitled "Tc-99m Glucoheptonate in Brain-Tumor Detection: An Important Advance in Radiotracer Techniques," again compares TcGH to TcO_4^-, with the finding that TcGH is superior to TcO_4^- for the detection of CNS tumors (*7*). The authors did not find this to be true, however, for the detection of cerebral infarction, an observation not entirely in agreement with that of Waxman and Rollo (*4,6*). Leveille et al concluded that compared to early brain scans, delayed studies frequently provided improved lesion detection, and they observed a progressive accumulation of TcGH in primary and metastatic tumor at 4 hr and even up to 9 hr after injection. It is not clear from their data whether improved detection with time represents an increase in the target-to-non-target ratio only, or an absolute increase in the radiopharmaceutical within the tumor. Relying on lesion-to-calvarial ratios, increases in target-to-non-target ratios with time have been demonstrated previously with TcDTPA, as well as with TcGH (*3,4,8*). Of importance is the authors' proposed mechanism that TcGH functions as a substrate for the highly metabolic brain tumor tissue, which results in an enhanced lesion uptake. Significant concentration of Tc chelates in lesions may be related in part to the increased metabolic activity of abnormal tissue. Mechanisms such as enhanced blood clearance, effective penetration of the blood/brain barrier, tissue binding, and other factors, however, must be considered.

We have recently analyzed 800 consecutive brain scans using TcGH, and have found the tumor detection rate to be 94%. The detection rate for infarction was slightly greater than 50% within the first week after insult, and increased to 75% after the first week. When a flow study was included, the detection rate for all infarcts was further increased to 90% (*9*).

Leveille et al have succinctly shown that for the detection of brain tumors TcGH offers certain advantages over TcO_4^- (*7*). Their paper should serve as a stimulus for the development of new radiopharmaceuticals, especially those agents which may combine several mechanisms, including that of substrate utilization.

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