

TRACER KINETIC STUDIES OF GLUCOSE TRANSPORT AND METABOLISM USING FLUORINE-18 - FLUROSUGARS IN ISOLATED RAT HEARTS

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Aspects of tracer kinetic compartment models for estimation of transport and metabolism of fluorosugars in isolated rat hearts were investigated. The positron emitting fluorosugars (¹⁸F)-2-deoxy-2-fluoro-D-glucose (2FDG) and (¹⁸F)-3-deoxy-3-fluoro-D-glucose (3FDG) were evaluated. These fluorosugars are transported by the cell membrane, but only 2FDG is significantly trapped by phosphorylation. Efflux of unmetabolized 3FDG might allow for regional quantitation of glucose transport rates by positron emission tomography (PET).

Tracer kinetic data were obtained using bolus injections of fluorosugars and coincidence counting of positron-electron annihilation photons from (¹⁸F) decay. A multi-compartment model that partitioned heart radioactivity into capillary, interstitial, cellular, and phosphorylated components was developed. Computer methods for estimation of model parameters were thoroughly studied. Physiological aspects of this model were tested by independent measurements of glucose consumption, chromatographic analysis of tissue for phosphorylated and free fluorosugar, and demonstration of competition of these fluorosugars with glucose for membrane transport.

Results of this investigation indicated that both 2FDG and 3FDG were transported and phosphorylated in the rat myocardium. The transport and phosphorylation rates of 2FDG were identical to those for glucose, while the 3FDG transport rate was one-half, and the phosphorylation rate one-tenth that of glucose. The dephosphorylation rate of 3FDG was twice that of 2FDG. Mutual inhibition of transport of 2FDG and 3FDG versus glucose was demonstrated, confirming that these analogs are transported by glucose carrier molecules. Chromatographic analysis of heart and brain from rats injected with 3FDG showed that 3FDG was phosphorylated in vivo at detectable levels, but the major component was the unchanged 3FDG.

The measurement of glucose transport rates by PET with 3FDG will require a dynamic scan approach, unlike the single scan approach currently used for estimation of glucose utilization rates with 2FDG. The low phosphorylation rate of 3FDG in cells should not interfere with the estimation of glucose transport rates, if the time required to obtain the necessary data is short. The slower transport rate of 3FDG, as compared to glucose, may be beneficial for the slow scanning techniques of PET, as corresponding transport rates of 3FDG in vivo are also slower.