

the highest average fraction of labeled cells. The pathologist scoring the immunohistochemical data (R. A. S.) was blinded to the FLT PET results. This same immunohistochemistry method was used and reported previously by our group (44).

Flow Cytometry. To provide for a meaningful comparison of SPF and Ki-67 scores, the area of a tumor selected and scored for Ki-67 immunohistochemistry was marked on the MIB-1 stained slide. This mark was then used to orient the paraffin tumor block so that two 60- μ m thick slices of the block could be recut for processing by the flow cytometry laboratory

cells within each lesion. The results reported here represent the SPF

maximize patient enrollment and compliance with the imaging protocol. We also quantitated FLT uptake with a Patlak determination of FLT flux from complete dynamic data to assess the incremental benefit gained from a more extensive imaging and analysis approach.

Tumor proliferative rates may be estimated in human tumor samples by mitotic figure counting, immunohistochemical detection of cell cycle-specific proteins (Ki-67 and PCNA), and the SPF determination from DNA flow cytometry. However, mitotic figure counting is affected by interobserver reproducibility problems, use of mitotic indices *versus* mitotic indices

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throughout S phase and G2, reaching maximum levels during mitosis (60). Therefore, the SPF is unlikely to be an optimal proliferation index for correlation with TK1 activity or FLT uptake. This is corroborated by the results of Rasey *et al.* (33) who showed that growth-arrested A549 cells stimulated to grow in fresh medium, demonstrated increased FLT uptake and increased TK1 activity with essentially no movement of cells from G₁ into S phase after 12–14 h.

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