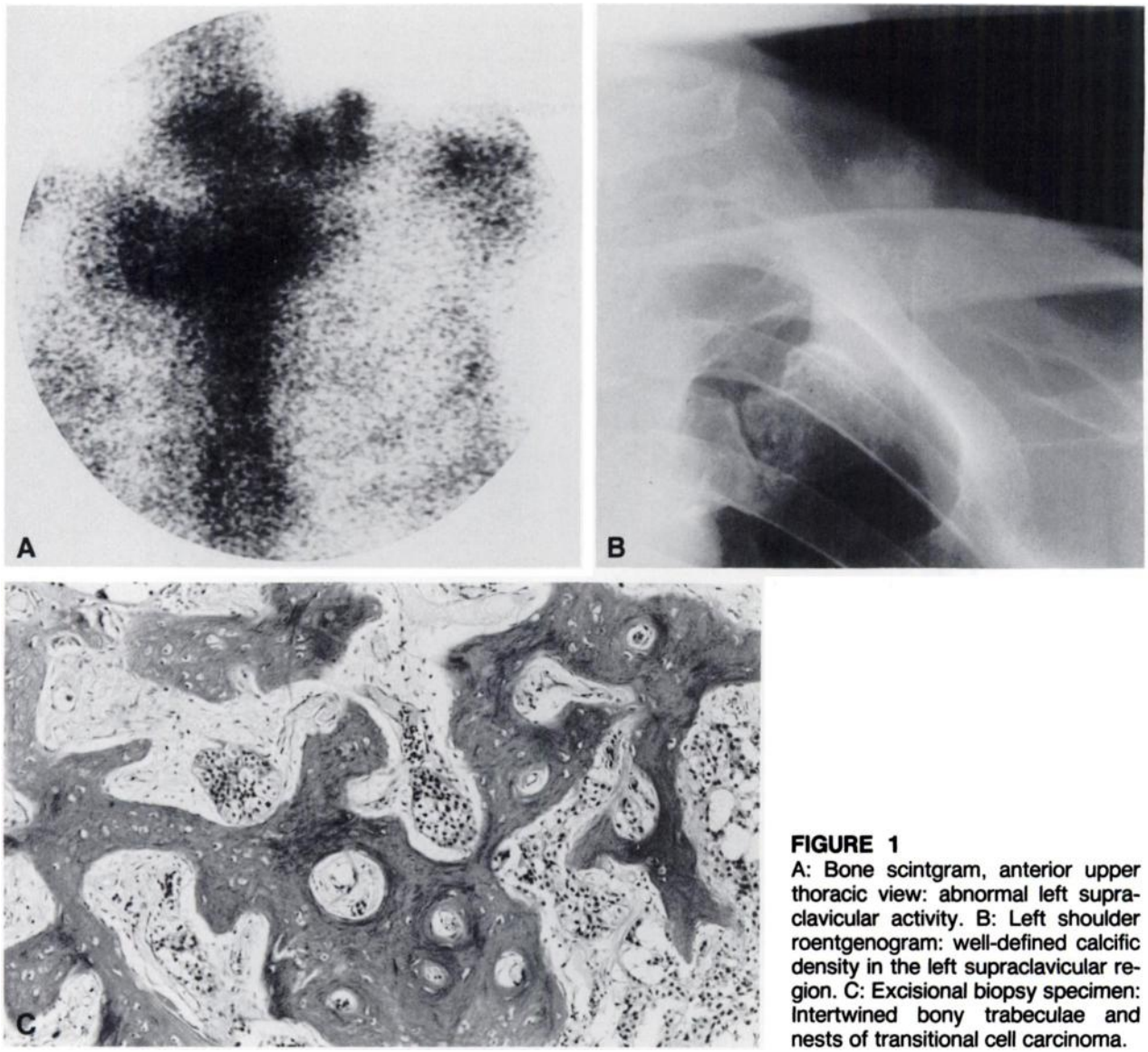

FIGURE 1
A: Bone scintgram, anterior upper thoracic view: abnormal left supraclavicular activity. B: Left shoulder roentgenogram: well-defined calcific density in the left supraclavicular region. C: Excisional biopsy specimen: Intertwined bony trabeculae and nests of transitional cell carcinoma.

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Tumor Uptake as a Function of Mass: Basis in Blood Flow

The interesting report by Williams and associates (*1*) on tumor uptake, can be placed into context by noting that aside from rare cases of material delivery by lymphatic, ascitic or other fluids, we are dealing with blood flow to tumors and

subsequent extraction. We have shown, as a reasonable first assumption, that the specific rate of change of blood flow (dF/F) can be set proportional to the specific rate of change of tumor weight (dW/W) (*2*).

$$dF/F = p \cdot dW/W \quad (1)$$

This integrates to a form identical to Williams' power law.

$$\log F = {}^{p} \cdot \log W + \log B \quad (2)$$

$$F = B \cdot W^{p}. \quad (3)$$

The exponent p was in the range of 0.52–0.64 for three reported series of tumors, and considerably higher for three others. At one extreme, tissue growth and metabolism might be limited by nutrient supply across the surface. This assumption leads to equations descriptive of fetal and placental growth (*3*). Larger values of the exponent (p) might be related to membrane infoldings and a functionally expanded surface area. It is also possible that the value of p may be viewed as a fractal dimension which can exceed the topological dimension [see for example, a discussion in (*4*)].

Williams and co-workers (*1*) also speculated on differential sensitivity, noting that poorly perfused volumes would be the most radioresistant. An approach has been made by means of dual radiotracers, one for blood flow and one for nutrient extraction (*5*). As blood was being supplied from the surface of the tumor, the "blood flow/gm of tumor decreases as the center of the tumor is approached" (*5*). A corollary was that the nutrient extraction/gram of tissue was also changing from the center of the tumor outward. Thus, approaches to quantifying blood flow may provide a basis for examining extraction of molecules by tumors.

Acknowledgment

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REPLY: We would like to thank Professor Spencer for his data and comments on tumor blood flow. His work clearly demonstrates the correlation of flow (ml/min) with tumor mass (W). We remarked on the necessity of tumor blood flow for tracer uptake (*1*), but wish to emphasize that its presence is not a sufficient condition for tracer accumulation.

Beyond gross size effects, which may prove amenable to fractal analysis, several additional reasons can be postulated for the observed slope (p − 1) variation. Aside from geometric differences between lesions of various shapes (*1*), there is a possibility of evolutionary changes as clones of the same tumor are differentially passaged through animals at a given laboratory. Thus, the slope may reflect a history-dependent as well as a tumor-dependent variable. It may occur that more than one type of clone is present in a particular experiment so that the resultant slope is simply a local average. In the presence of carrier material (e.g., cold antibody), there is an additional complication involving competition between label and carrier for a limited number of target sites in the tumor. Here the uptake may be expected to decrease at lower masses since the amount of cold material might be sufficient to saturate minute lesions and effectively exclude the label. The signature of such an event is a much flattened uptake-versus-mass curve; i.e., one having a slope close to zero. Researchers advocating the use of relatively large amounts of carrier protein in monoclonal experiments should be aware of this possibility. This is an example where uptake is not correlated with flow and could approach zero as tumor size decreases.

One should mention the consideration of time variability in the biodistribution results. A typographic error in our original article (*1*) must be corrected to read that all biodistributions included therein were obtained at times *greater* than 24 hr postinjection of the tracer compound. If one is forced to compare data taken at greatly different times, a correction for reduced uptake and/or clearance also may be necessary.

Acknowledgment

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Technetium-99m Compounds for Measurement of Cerebral Blood Flow

TO THE EDITOR: Scheffel et al. (*1*) reported on potential technetium-99m-labeled diaminodithiol ([^{99m}Tc]DADT) derivatives for measurement of cerebral blood flow focuses on a 4′-methyl-N-ethyl-piperidinyl isomer with marked lipophilicity having an octanol:water partition coefficient P of 1671 (log P = 3.22). This means that the tracer is probably not completely extracted in the brain, as binding to proteins in plasma and erythrocytes will impede the transfer across the blood:brain barrier (*2*). In this situation the observed slow