Radiation Lung Damage Causes Increased Alveolar Permeability Leading to Increased Clearance of Technetium-99m-DTPA

TO THE EDITOR: Webster's dictionary's definition of *impair* is "to damage or make worse by or as if by diminishing in some material respect" (*1*). The synonym is *injure*. The article by Susskind et al. (*2*) contains in its title the phrase *impaired permeability*, which is ambiguous, if not misleading. According to their results, radiation-induced lung injury decreased the $T_{1/2}$ of ^{99m}Tc-diethylenetriamine pentaacetate aerosol (DTPA) clearance, which speaks for enhanced permeability.

We found results similar to those of Susskind et al. in a study of 36 patients (*3*). More than 15 min decrease in $T_{1/2}$ of ^{99m}Tc-DTPA aerosol clearance compared to the preradiation $T_{1/2}$ predicted radiation pneumonitis but was not specific. Susskind et al. state that their findings are consistent with Ahmed et al. (*4*). In a canine model, Ahmed et al. measured postradiation ^{99m}Tc-DTPA aerosol clearance and found an increase in the $T_{1/2}$ of ^{99m}Tc-DTPA aerosol clearance (decreased clearance and decreased permeability). The findings of Ahmed et al. are contradictory to the findings of our study as well (*3*). That was one reason our study was not published as a full-length article. There are numerous differences in the studies of Ahmed et al. and Susskind et al. and our study. Ahmed et al. irradiated the normal canine lung and compared the results with contralateral normal lung. We and Susskind et al. mainly looked at the lung adjacent to the radiation field because the tumor area directly in the radiation field did not have significant aerosol deposition.

It is encouraging to see that our results have been confirmed by Susskind et al. However, the use of terms such as *altered* or *impaired* that carry ambiguous meanings can confuse or mislead readers. Radiation lung damage causes increased alveolar permeability, leading to increased clearance of ^{99m}Tc-DTPA, and, consequently, decreases the $T_{1/2}$.

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REPLY: We thank Drs. Halkar and Camarano for their comments concerning our article, "Impaired Permeability in Radiation-Induced Lung Injury Detected by Technetium-99m-DTPA Lung Clearance" (*1*).

Without getting into a question of semantics, we selected the words for our title, including the word *impaired*, very carefully. However, as we and others have shown, radiation-induced impairment can be reflected not just by an increased permeability but by a decreased permeability as well. Part of our article was the documentation that both types of impairment occur at different times in the same patient. While radiation did reduce the mean values of $T_{1/2}$ of the ^{99m}Tc-diethylenetriamine pentaacetate aerosol (DTPA) lung clearance of patients with radiation pneumonitis after ~50 days (Figs. 2 and 4), in several of these patients the values of $T_{1/2}$ during radiotherapy were also increased (Fig. 1). Similarly, the mean values of $T_{1/2}$ for patients without radiation pneumonitis were increased as well as decreased (Figs. 2 and 3).

Our results showed that very early changes such as increases and decreases in permeability occurred during radiotherapy and these changes could be measured before detectable alterations were observed in CT scans and chest radiographs. It is in this context that we compared our results with those of Henschke et al. (*2*) and Ahmed et al. (*3*). Henschke et al. measured changes in the MR signals of patients during radiotherapy that reflected an exudative process and reduced permeability. This is similar to the exudates and hyaline membrane formation found by Ahmed et al. after a high, single-fraction radiation dose to dogs and also reflected reduced permeability. However, Ahmed et al. (*3*) also found very sharp increases in permeability again after the second week postirradiation in several dogs.

We also found from lung images that DTPA deposited in the lungs, within the radiation port, in most patients. This allowed us to compare the DTPA clearance from the shielded as well as the irradiated lung regions. We could, therefore, conclude that the response was systemic.

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Cerebellar Metabolic Reduction in Alzheimer's Disease and Data Normalization

TO THE EDITOR: We read the article by Ishii et al. (*1*) with interest. As cited by Ishii et al., Alzheimer's disease (AD) is a neurodegenerative disease that affects the brain globally, but heterogeneously, even involving the cerebellum in certain cases. Based on their finding of cerebellar metabolic reduction, the authors conclude "there may be no regions in the brains of AD patients that could be used as a good reference region for normalizing" (*1*). We agree that data normalization in functional brain analysis must be treated with care and interpreted with caution.

The necessity for data normalization often arises in a cross-subject comparison of nonparametric data such as diagnostic brain perfusion SPECT (*2*). A common objective in data normalization is to compare patient data to normal controls so that the presence of functional abnormality can be determined in a consistent manner. To delineate such functional changes, however, it is important to examine not only the magnitudes in changes but also their variability (*2,3*). Unfortunately, the latter issue was not addressed by Ishii et al. (*1*).

We previously examined glucose metabolism in 37 probable AD patients and 22 normal controls with and without data normalization (*3*). When analyzing data quantitatively, there was a 6% average metabolic reduction in the cerebellum of AD patients as compared to normal controls. In contrast, glucose metabolism was affected more severely in the parietotemporal cortex, which showed a 29% average reduction. When normalizing parietotemporal cortical activity to the cerebellum, this reduction became 25%, indicating an underestimate of the magnitude of the