As a consequence, sophisticated methods are mainly means of reducing the required individual therapeutic activity. A more interesting concept is that the dose distribution conditions the clinical outcome of AFTN patients far more than the dosing scheme. You probably misred Table 3, since we almost reached our intended absorbed dose of 80 Gy using the Marinelli method (mean 80.5 Gy to the whole thyroid, 72 Gy to the AFTN) in patients with no extranodular activity (no-ENA), although underdosing occurred in patients with ENA. At any rate, the mean absorbed dose to the extranodular lobe (8.5 Gy) was far from insignificant in no-ENA patients, and would have been more than 3-fold higher using 300 Gy, a dose level constituting a high risk for secondary hypothyroidism. ENA patients correspond to two subgroups of patients. Those with "compensated AFTN" can successfully be cured with a low intended absorbed dose and hence with low activities. Adjuvant thyroxine therapy may limit secondary hypothyroidism, as suggested in this paper, although we have no experience of this therapeutic modality. ENA patients with "decompensated AFTN" were shown to have unpalpable multifocal autonomy, because significant focal uptake and imaging could be evidenced in the non-AFTN lobe. This is highly consistent with the fact that hypothyroidism may not develop in such patients, despite a mean dose of 49 Gy delivered. Indeed, the nonuniformity of dose distribution will spare healthy tissue from the beta irradiation. Ultrasonography may depict millimetric nodules in areas showing evidence of scintigraphic autonomy (Fig. 1), although it is true that autoradiographic proof is mandatory for definite conclusions.

Our mortality estimates are very similar to those observed in Berne and are clearly higher than those of the matched control population in Paris (13.5% expected versus 22% in AFTN patients, $p<0.01$). As both our studies are retrospective analyses, however, the excess mortality may reflect a bias in the choice of the therapy because more severely ill patients are usually referred for iodine and not for surgery. Hyperthyroidism, which may cause cardiac complications, the main cause of death in AFTN patients, is more likely responsible for the fatal outcome than ^{131}I, because most of the patients died once cured and long after the therapy. Although large epidemiological studies serve to strengthen this point of view, there is still no definitive argument in favor of propylactic therapy for low toxic forms of AFTN.

The prevalence of antithyroid antibodies in patients with thyroid autonomy is low in Paris: antimicrosomial antibodies (ATPO not available at that time) were undetectable in 90% of patients, at the threshold (1/400) in 6% or slightly elevated in 4%. Finally the incidence of autoimmune thyroiditis after ^{131}I remains, at first glance, extremely low in this group of patients.

As epidemiological studies, the clinical presentation, and the molecular dissection show that thyroid autonomy is a moving spectrum of diseases, we think that a "best dose of 300 Gy" cannot be considered as a universal gold standard. We agree, and had suggested that the individual calculation of the activity, which can be done using early uptake values, remains interesting, mainly for radioprotection which is increasingly a public health concern.

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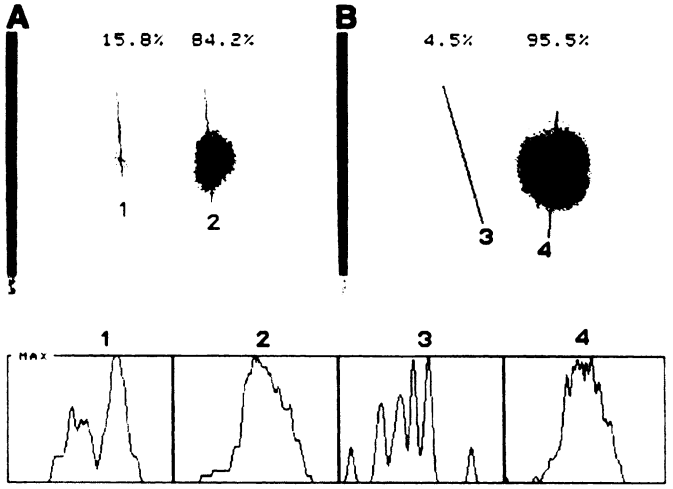

FIGURE 1. Two patients with left toxic AFTN (TSH<0.03 μU/ml) corresponding to a single palpable thyroid nodule. Patient A had evidence of ^{123}I activity in the right lobe which corresponds to at least two foci of autonomy, clearly visible on the radioactive profile 1. Ultrasonography depicted 4 millimetric nodules ranging from 3 to 7 mm. Patient B had a typical toxic adenoma with no significant activity in the right lobe (profile 3) which is homogeneous using US. Relative lobar counts are presented at the top of each lobe. Profile curves (P) are smoothed and normalized to their maximum (P1:8, P2:25, P3:3, P4:26).

Is Renography Suitable for Deconvolution Analysis?

TO THE EDITOR: The application of deconvolution analysis to a renogram is particularly attractive, as it theoretically allows one to obtain the spectrum of intrarenal transit time (*1*). Many reports have been published which assess the clinical value of transit parameters obtained by deconvolution, as well as reports describing methods for performing the deconvolution (*1–2*). Few authors, however, have addressed the central issue: whether or not a renogram is suitable for deconvolution analysis. Two conditions should be respected for deconvolution analysis to work: linearity and stationarity (*1*). By applying deconvolution to the renogram, we assume that, in the kidney, these conditions are fulfilled. During the last few years, however, evidence has accumulated which raises doubt about the validity of these assumptions.

- For some radiotracers commonly used for renography, the renal extraction rate may vary with time. This has been repeatedly demonstrated for iodine-labeled hippuran (*3,4*) and also, by some authors, for ^{99m}Tc MAG3 (*4*). It is obvious that the modification of extraction efficiency invalidates the stationarity condition.
- For the deconvolution of a renogram, a precordial curve is usually used as the input function. It is well demonstrated that a precordial curve often differs from a plasma curve because of the interstitial activity included in the precordial region of interest (ROI) (*5,6*). Because tracer kinetics in the tissue differ from those in the plasma,

both the linearity and stationarity conditions no longer hold. The same occurs if impurities are present in the administered tracer.

- The output function used is the renogram containing both renal and nonrenal activities. For the deconvolution process itself, no problems arise as long as the included nonrenal systems respect the linearity and stationarity conditions. In the presence of liver uptake and biliary excretion, however, tracer kinetics inside the ROI are usually unpredictable and violate the stationarity condition. The same problem can also occur in instances of incorrect background correction.

The most important factor is the real output function of the kidney itself. The stationarity condition is broken down in many physiological conditions. Urine is transported from the renal collecting system to the bladder by active peristalsis initiated from a pace-maker in a minor calyx, and it has been shown experimentally that pelvic contractions could be erratic and discontinuous (*7,8*). Moreover, it has also been shown that pelvic contraction can be provoked by various physiological stimuli, including swallowing a small volume of water and anxiety (*8*).

Although a vesicoureteral reflux episode obviously invalidates the stationairity condition, physiological backpressure from the bladder also modifies the renal output function (*9,10*). George and O'Reilly (*10*) have shown that, even within physiologic limits, elevation or reduction of bladder pressure markedly affects renographic excretory function.

In summary, the application of deconvolution analysis to a renogram is confronted by many sources of error due to the violation of the linearity and stationarity conditions. The transit parameters obtained by deconvolution, therefore, do not correctly reflect the intrarenal transit time. This could explain the limited diagnostic yields of deconvolution techniques (*2*).

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Discriminant Value of Semiquantitative SPECT Data in Mild Alzheimer's Disease

TO THE EDITOR: The early identification of Alzheimer's disease with SPECT is an attractive challenge, as emphasized by the recent article of O'Mahony et al. (*1*) and the accompanying editorial. The high sensitivity and specificity reported by these authors, even in a prospective study of questionable dementia patients (CDR 0.5), are gratifying, especially considering their relatively simple image analysis. It is particularly surprising since their ROI definition plane appears to have completely missed the parietal cortex, identified by earlier investigators as heavily affected.

It is unclear to me, however, that their discriminant function was important to their success. At the outset of their Discussion, the authors state that the 'use of single SPECT-derived temporoparietal perfusion measurements is not sufficiently sensitive to be of diagnostic value.' Similarly, in the first paragraph of the Results section, the authors state that the posterior temporal region was most effective in discrimination of the two groups, but 'there is a significant degree of group overlap.' These statements are not corroborated by any data, other than their raw observations in their in Table 4. It would be helpful to actually have the overlap and discriminability numbers.

An examination of the discriminant function coefficients in Table 4 raises more concerns. The strongest positive predictors are the left posterior and right anterior ROIs; the left anterior ROI is actually a negative predictor. Thus, the strongest association with an Alzheimer's disease diagnosis would be established for a patient with relatively low perfusion in the right anterior and left posterior temporal regions and relatively high perfusion in left anterior temporal regions. Such a peculiar network of cerebral deficits has never been described before, to my knowledge, in SPECT observations or any other dataset.

Finally, the validity of the proposed LDF would be enhanced if the authors could show correlations with severity of disease, e.g., the MMS. If such correlations are unimpressive, and if the authors can offer no theoretical or empirical corroboration for this particular network, I would suggest that we are observing here the known power of discriminant function analysis to capitalize on random noise in small samples (despite the jack-knife procedure). Perhaps the data can be strengthened, and the negatively-loading regions removed, if the parietal cortex were included by analyzing an additional, higher slice.

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