Imaging of Breast Hormone Dependent Tumors

In the July issue of the Journal Spicer et al. observed "If the association between Br-77-E1 and estrogen receptors can be demonstrated in human patients it may be possible to define, in vivo and preoperatively, which patients have a high probability of responding and which have little chance of responding to endocrine therapy" (1). Since 1977 (2) we have studied about five patients a week by a similar method in our laboratory.

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REFERENCES

Reply

Dr. Skromne-Kadlubic has brought to our attention his work with I-131 labeled "estrogenic complexes" (1). Using "estrogenic complexes" labeled with I-131, seven of seven estrogen receptor positive tumors were visualized while eight of eight estrogen receptor negative tumors were not visualized. These are excellent results especially for high background, low contrast images. It is important to identify the exact molecule localizing in the tumor. Neither the chromatographic uniformity nor the structure of the "estrogenic complexes" is mentioned. Komai and Eckelman (2) show a variable stability of the I-131 steroid bond associated with several different steroids. We considered using I-131 as a label but evidence suggests that iodination of a steroid often yields a radiopharmaceutical that is less than optimal (2,3). From physical/chemical calculations the C-I bond strength is 53 Kcal/mole while the C-Br bond strength is 67 Kcal/mole. This basic physical/chemical fact is the reason for bromine having chemical superiority over iodine. The stability of our Br-EI, Br-E2 is supported by chromatography (4). The relative in vitro and in vivo instability of the iodine label is becoming evident; it appears that a nuclide of bromine may be more suitable for use with steroids (5).

The exact localization of our radiotracer has yet to be determined. Since breast cancer may be characterized by the presence or absence of estrogen receptors it is reasonable to believe the major determinant of tumor visualization by imaging is the relative concentration of estrogen receptors. Dr. Skromne-Kadlubic's results suggest this may be so. Unfortunately the presence of estrogen receptors is not unique to hormonally dependent breast cancer (6). Even with high blood clearance rates the target-to-background ratio is low.

We have imaged four patients, visualizing two of three estrogen receptor positive tumors and not seeing increased Br-77-E1 activity in the one patient with an estrogen receptor negative tumor. These results have been encouraging but more radiotracer development work and subcellular localization studies must be performed to clarify the method and site of localization.

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REFERENCES

Serum TSH Levels in Therapy of Thyroid Carcinoma

With regard to radiiodine therapy for thyroid cancer Hilts et al. (1) draw conclusions that their data do not support. Their data indicate how long it takes to achieve an elevated serum TSH level after withdrawing thyroid hormone and conclude that radiiodine therapy should be given at that time. They apparently do not consider that it is desirable for residual thyroid cancer to be subjected to the influence of high TSH levels for some period of time (3 wk) to assure that uptake of the radiiodine is increased as much as possible. It is for this reason that the accepted protocol is a period of 6 wk off T4 before treatment, approximately 3 wk to deplete the thyroid hormone from the circulation and 3 wk to permit high TSH stimulation of the residual tumor. By shortening the period of hypothyroidism, it is possible that Hilts et al. are increasing the probability that their patients will have to comply with "repeated courses of radiiodine to ablate residual or metastatic cancer." Perhaps they would be able to successfully eliminate residual uptake in most patients with a single treatment as has been our experience. The use of diuretics and diet to deplete stable iodine prior to radiiodine therapy may be helpful in this regard (2).

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Reply
We have found no data in the literature to support Dr. Ham-
burger’s assumption that in metastases radiiodine uptake will
continue to increase with prolonged exposure to high TSH levels.
Although this is a theoretical possibility, there are practical reasons
for minimizing the duration of hypothyroidism. Protracted hy-
potyroidism is poorly tolerated by patients, it may have medical
complications and it may be associated with tumor growth. Ac-
cordingly, we have chosen to administer radiiodine at the time
of maximal pituitary TSH secretion and to keep the period of
hypothyroidism as short as possible.

After thyroidectomy residual uptake of radiiodine in the thy-
roid bed is usually associated with residual normal, functioning
thyroid tissue. Such uptake can often be ablated with a single dose
of I-131. Successful ablation of thyroid bed uptake should not be
confused, however, with eradication of uptake in functioning
metastases; the latter often requires repeated treatment with I-
131.

Low iodine diets may augment tumor uptake of I-131 by de-
creasing the amount of stable, carrier iodine in the body; such diets
require rigid patient compliance in view of the widespread intro-
duction of iodine into food and food additives. The use of etha-
crynic acid to deplete body iodine as advocated by Hamburger (1),
however, may cause serious side effects. Nemec et al. reported
clinical intolerance to ethacrynic acid pretreatment such as
drowsiness, muscular weakness, arterial hypotension, and mani-
festations of previously latent tetany (2). When ethacrynic acid
is stopped renal iodide clearance falls sharply, which results in
increased body retention of I-131 and increased whole body ra-
diation; this effect is independent of I-131 uptake in the tumor. As
Sisson has observed, a similar effect of increased tumor and whole
body radiation can be achieved simply by increasing the dose of
I-131 (3).

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Glucocorticoid Kidney Studies

The comparison of Tc-99m glucocorticoid renal imaging with
the i.v. urogram for the detection of mass lesions, reported by
Leonard et al. (1), was impressive (accuracy 85% against 71%).

Since their findings confirm my impression and that of many other
clinical groups using Tc-99m glucocorticoid since 1974, it is
surprising that no previous report on glucocorticoid imaging has
appeared in the medical literature. (Glucocorticoid has been re-
ported to be equivalent to iodinnopurate for the evaluation of renal
function (2).) This report (1) with its excellent results is, therefore,
particularly welcome, since one is reluctant to recommend a new
procedure over a well-established test solely on the basis of anec-
dotal experience. The report was incomplete however, and the
results as reported were almost certainly less favorable to glu-
cocorticoid than actual clinical experience would indicate, consid-
ering that six of 47 cases were excluded because urograms were
considered inadequate for interpretation.

It would be of interest to know what occurred in the clinical
setting, in addition to the reported results of comparative evalua-
tion later “reviewed independently by two observers without benefit
of clinical history.” How were the 47 radiographic and radionuclide
studies initially reported, and how did this affect clinical mani-
gement? Were six to eight urograms initially considered inade-
quate and a radionuclide study therefore recommended? If the
initial diagnostic study, whether radiographic or radioactive, were
considered adequate, why was the other study done? Unless this
was a prospective clinical research project, the second study should
have been considered redundant, before knowing the results of this
comparison report. What were the clinical indications for these
studies and in the other patients who had glucocorticoid renal
imaging alone? I doubt that a scan would have been preferred
initially over i.v. urography (IVU) for suspicion of neoplasm.
Herefore, the most common indication for radionuclide studies
has been inability to perform IVU because of either allergy to iodo-
ine or impaired kidney function; less commonly to determine the
cause of impaired function, or of hypertension, of the vascularity
of a lesion demonstrated by IVU; or to evaluate other aspects of
function, such as obstructive uropathy.

The authors (1) state that the radionuclide flow study was not
found “to be reliably helpful in evaluating the vascularity of mass
lesions.” They must mean that a cyst may mimic a mass lesion, as
has been reported previously. How accurate was the flow study in
differentiating cysts from mass lesions? I have found the flow study
extremely important in this regard; including one patient with
hypertension shown to have a highly vascular kidney lesion, said
to be a cyst by ultrasound but proved to be hypernephroma. (Ul-
trasound was redundant as well as wrong in that case, since biopsy
is indicated unless a lesion appears avascular as well as cystic by
ultrasound.)

The authors (1) suggest the possibility of missing extrarenal
disease if only radionuclide studies are performed, but add that
no significant extrarenal disease was detected by IVU in their
cases. In how many of their patients was significant extrarenal
disease detected in radionuclide studies? In one published report,
clinically unsuspected significant findings were discovered in 22%
of patients by radionuclide studies (3). I continue to be amazed
at the high incidence of significant incidental findings in Tc-99m
kidney studies, visualized primarily in a vascular flow study. Two
of the most striking examples have been published (4,5). I have
also found aortic aneurysm and pseudo-aneurysm; extrarenal
neoplasm, inflammatory disease, and hematoma; and occlusive
peripheral arterial disease. Conversely, when the vascular flow
study has been done to evaluate arterial disease, kidney abnor-
malities are often discovered.

I am sure that Dr. Leonard’s article will encourage more ex-
tensive use of this important diagnostic modality, and I hope other
groups will evaluate their experience with Tc-99m glucocorticoid
kidney studies for publication.

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