Thyroid Scanning of the Patient with History of Childhood Irradiation

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ABSTRACT

The utilization of external radiation for the treatment of benign conditions of the head and neck is no longer employed because of the discovered association of local irradiation with the development of thyroidal cancer. This practice was widespread until two or three decades ago. It is also known that there is a very long latent period between previous radiation and the development of thyroid cancer. In consequence, a substantial number of persons can be expected to develop thyroidal malignancy each year until the turn of the millennium, and even later. If this association is real, then early diagnosis is especially important because of the excellent therapeutic results that can be obtained with early diagnosis. Physical examination performed on a regular basis is the most important single diagnostic aid. A statistically significant improvement in sensitivity is obtained when palpation is performed in conjunction with radioisotopic thyroid scanning. The scan helps by identifying areas of abnormality and—even more importantly—by allowing distinction of those nodules which are hypofunctioning and thus more likely to be malignant.

Introduction

Until recent years, external radiation was frequently administered to reduce the size of enlarged thymus glands or for the treatment of tonsillitis, adenoiditis, cervical adenitis, hearing loss, hemangioma, acne, scalp infections, keloid, and for a variety of other benign conditions. During the course of these treatments, the thyroid gland was frequently exposed to direct or scattered radiation.

External therapeutic radiation for these benign disorders was an accepted practice until the wide availability and use of antibiotics and until the revision of previous theories in the early 1950's regarding the relative insignificance of thymic enlargement. The first report concerning a possible association between neck irradiation and thyroid cancer appeared in 1950. Since then a number of epidemiological and clinical studies have established a correlation between thyroid neoplasia and previous irradiation.

It is estimated that there are over a million individuals in the United States alone who have received radiation for benign conditions of the head and neck. The risk that any one such individual will develop a subsequent malignancy is approximately 7 to 9 percent. A number of variables, such as age and radiation dose, govern the induction of cancer in humans fol-
lowing radiation. Several experimental studies have demonstrated that a special promoting factor in thyroid neoplasia is the presence of elevated levels of thyroid stimulating hormone (TSH)—either caused by goitrogens or secondary to decreased thyroid function following radiation. The adverse effects of radiation, in this context, are due not only to its direct carcinogenic effect on tissue, but also to the action of an increased TSH level resulting from radiation induced cell death.

Most of the neoplasms which develop are readily detected and are benign. Less frequently, malignant neoplasms are identified. These are almost always (90 percent) papillary or less commonly follicular adenocarcinomas. They tend to be of low grade malignancy which grow slowly and can usually be controlled or cured with appropriate therapy. No anaplastic or medullary tumors have been described. The latent period between radiation and the development of overt thyroid diseases may be as short as five years or as long as 40 years.

**Diagnosis**

A number of guidelines and protocols have been developed for both hospitals and individual physicians for the screening of exposed individuals and for public education. All of these place great emphasis on careful history taking and physical examination. The clinical study of Favus et al demonstrated the contributory role played by thyroid scanning. This showed that patients whose thyroid was examined without prior knowledge of the scintigram revealed nodules in 141 instances, re-palpation following examination of the scintigram disclosed nodules in an additional 33 patients. However, it is important to note that this study, like many others, was uncontrolled for the occurrence of abnormal scintigrams in non-irradiated populations. Arnold reported, in his study of 1452 persons, a detection rate by scintigraphy as high as 96 percent of surgically proven nodules, —40 percent of which could have been missed if a physical examination alone had been done.

**Technique**

The rationale for the use of radioiodine or technetium as imaging agents when searching for thyroidal malignancy rests upon the ability of the techniques to identify the level of functional activity in an individual nodule. This information is important because of the observation that approximately 16 percent of all solitary hypofunctioning nodules in a non-exposed population are malignant. This figure is dependent upon the clinical behavior of the "cold" nodule; the incidence of malignancy in clinically benign nodules is 0 to 6 percent; in possibly malignant nodules is 12 to 28 percent; and in probably malignant nodules is 53 to 74 percent. A recent report by Blum et al gives the impression that these numbers might also be true for radiation-exposed populations. By comparison to the experience with "cold" nodules, functioning nodules—either "warm" or "hot"—are very rarely malignant.

There is considerable confusion regarding the pathologic significance of the functional level of thyroid nodules and the influence of factors such as nodule-number and radiation history. In a recent report, Sisson et al point out that only one or less out of every thousand malignant nodules exhibit function when imaged with radiiodine. If the fraction of benign nodules which concentrate radioiodine were conservatively estimated at 1:5, then according to Bayes' theorem, the posterior probability of any given functioning nodule being benign is 99.79 percent. The frequency of cancer in non-irradiated thyroid glands having a multinodular scan appearance is only about 5 percent.

It is most important to be aware of a history of prior radiation because this raises the incidence of carcinoma in multinodular glands to approximately 47 percent. Also, it is widely believed that approxi-
mately 33 percent of isolated “cold” nodules with a history of x-ray therapy are cancerous.6

Nodules which are not visualized by scan have been called “non-delineated”22 and these are less likely to be malignant than are hypofunctioning (“cold”) nodules.15 According to Charkes,8 the reported frequency of cancer in non-delineated nodules is 3 to 8 percent. It should be emphasized that oblique pinhole gamma camera views are essential for the differentiation of “nondelineated” nodules from true “cold” and “warm” nodules.

The element technetium, in its radioactive form of 99m Tc O₄⁻, has been found to be an excellent thyroid imaging agent,12,16 since it appears to be concentrated by a similar trapping mechanism, as is iodine.2 Because of its favorable physical characteristics, 99m Tc O₄⁻ is usually preferable to 131-I for the majority of patients. However, there are certain exceptions which relate to the fact that 99m technetium pertechnetate only yields information concerning the trapping function and not the organification phase of thyroid metabolism. A number of reports4,29,31 describe disparities between the results obtained by technetium and by iodine scanning techniques. Not all nodules which appear “cold” on radioiodine images appear “cold” on technetium scans; some may even appear “hot” or “warm.”

This can be explained on the basis of dissociation between the trapping and organification functions of the gland. Thus, nodules which fail to concentrate radioiodine — and by implication may be malignant — might be subrogated to the non-malignant category if imaged with technetium alone. However, each of the radioisotopes of iodine has drawbacks regarding physical properties, economics of production, shipment, and radiation dosimetry. Only four radioisotopes of iodine, viz., 123I, 125I, 131I, and 132I, have been utilized by clinical imaging. In table I is shown information regarding the radionuclides which are currently used for thyroid imaging.

Of the three nuclides of iodine currently available, 131I represents the best combination of radiation dose, photon flux, and optimal gamma photon energy. 131I, although still widely used, is not appropriate for screening a population already at risk from previous radiation. Furthermore, the primary photon emitted by this
nuclide is poorly absorbed by the thin (12.5 mm) crystal of the gamma camera. $^{125}$I is unsuitable because of its low photon energy and high radiation exposure. Commercially prepared $^{123}$I may contain significant amounts of impurities, such as $^{124}$I, $^{126}$I, $^{131}$I, and $^{130}$I. These increase the radiation dose to the thyroid and degrade the image by septal penetration of high energy photons. The amount of these radionuclidic impurities in commercial $^{123}$I measured within two to three hours of calibration time is: $^{130}$I-less than 3 percent; $^{124}$I-less than 1 percent; $^{131}$I-less than 0.5 percent; $^{126}$I-less than 0.5 percent.

Increased emphasis placed on the need for improved ability to detect small lesions has led to the widespread utilization of the gamma camera fitted with a pinhole collimator. However, pinhole collimators introduce moderate to severe distortion of perspective and sacrifice counting efficiency for gain in spatial resolution and field size enlargement. Moreover, the contaminants in commercially available $^{123}$I preparations are less able to penetrate the thick walls of the pinhole collimators than the conventional multi-hole collimator. Besides the standard anterior views taken with anatomic markers to judge size, additional views in the right and left anterior oblique projections may be needed to evaluate fully the palpable nodules which may not be seen on the anterior view alone. These additional oblique views also help to confirm or exclude doubtful abnormalities seen on the anterior view, as was discussed previously. It is important to evaluate only the right lobe on the right oblique view and the left lobe on the left view, because the contralateral lobe very often appears distorted owing to shortcomings inherent in the pinhole collimator design. In our experience, lack of attention to this point can lead to false positive interpretation. The development of tomographic imaging techniques using multiple pinhole collimators shows promise for improved visualization of small thyroid nodules.

### Management

Although there are many variations in detail, two major recommendations emerge from the survey of current practice. Firstly, suppression of endogenous TSH production is widely recommended for all persons known to be at risk from prior radiation. This is easily achieved by the daily administration of a small (100 mg) dose of exogenous thyroxine. This type of therapy is reserved for those patients with diffusely enlarged thyroid glands. In our experience, this is seen in only eight to ten percent of irradiated persons. Secondly, periodic physical examination is recommended with special attention to a meticulous palpation of the thyroid gland. This should be performed on an annual or biennial basis. A scan should be performed at the initial visit and, subsequently, whenever a nodule is suspected or identified by clinical evaluation. It is recommended by us that ultrasound examination of all "cold" nodules with needle aspiration be performed when the nodule is cystic. These recommendations are summarized in figure 1.

### Discussion

The inclusion of a diagnostic procedure involving the use of ionizing radiation in the screening of individuals believed to be at risk from previous radiation raises both moral and ethical questions. It must be made certain that the radioisotope does not constitute a further hazard to the pa-
tient. Radioiodine has been in use for approximately a third of a century as a therapeutic agent for hyperthyroidism. For this purpose, considerably larger quantities are employed than for scanning. Even with this extensive experience, there is little firm evidence that it constitutes a carcinogenic risk to adults.10

On the other hand, large quantities of externally administered radiation have been conclusively demonstrated to represent a carcinogenic risk by the Atomic Bomb Casualty Commission. There are also scattered case reports of the development of thyroid cancer many years after external irradiation to the adult neck for therapy of non-thyroidal conditions.5'18 Despite the absence of any evidence linking the small doses of radioisotope used for scanning with the development of cancer, a deliberate effort is made to minimize radiation exposure. Because the radiation dose to the thyroid and whole body is significantly lower with 123-I and 99m-Tc than with 131-I, it is recommended by us that the latter agent no longer be used for routine thyroid imaging (table I). Ultrasonographic examination of the thyroid has proven to be an excellent method for the delineation of thyroidal anatomy and for the differentiation of cystic from solid structures.

Even though this technique does not yield functional information, such as that obtained with radionuclide scanning, ultrasound is the single most valuable follow-up study for evaluation of "cold" nodules. This is because the probability of cystic nodules being malignant is significantly lower than with either solid or mixed cystic/solid nodules. Sisson et al30 have used Bayes' theorem to show that a "cold" nodule, which is purely cystic on ultrasound examination, has a 99.72 percent probability of being benign.

The technique of fluorescent thyroid imaging is based on detection of the small amounts of non-radioactive iodine (127-I) which are present in thyroid tissue. Although this procedure is currently available in only a few centers, it constitutes a promising new addition to the diagnostic armamentarium.

In conclusion, it should be mentioned that Royce et al have recently failed to find an increased number of thyroid abnormalities in a group of patients who had received prior irradiation to the head and neck.27 Thyroid cancer was detected in only one of 214 irradiated persons and in two of 243 controlled subjects. Thus, the entire question of carcinogenicity of external therapeutic radiation to the neck has been re-opened. The authors fully agree with Utiger that other recall programs should include a well controlled simultaneous examination of non-irradiated subjects.32

For the individual physician, these data once again emphasize that a physical examination alone should be performed during the initial and follow-up visits. Thyroid scans, other tests, or thyroid hormone therapy are unwarranted unless a palpable thyroid abnormality is found.

**Summary**

Radioisotopic scanning can help in the early detection of thyroid nodules and in the identification of those which are more likely to be malignant. The technique employed is of paramount importance. Using the best instrumentation and radionuclides, nodules as small as five millimeters may be easily detected. The entire procedure is noninvasive, can be performed at a single visit, and is relatively inexpensive. For individuals at risk, an initial scan will help the clinician in his physical examination. The radiation dose from this procedure is acceptably low, and the only known relative contraindications are pregnancy and lactation.

**References**


