# A Perspective on Post-Chernobyl Radioablation in Young Females

In the article by Travis and Stabin in this issue of *The Journal of Nuclear Medicine* (*1*), the risk of breast cancer from radioiodine ($^{131}$I) ablation treatment in young females with thyroid cancer is discussed on the basis of dosimetric calculations. In the past, this issue was of minor importance, as thyroid cancer is rare in children and adolescents. In western countries, the incidence rate normally is 0.5−1 per million inhabitants per year. Soon after the Chernobyl accident, however, the incidence rate increased dramatically in regions with high fallout, such as Ukraine, Belarus, and some Russian oblasts. High activities of radioactive iodine in the fallout contaminated milk

See page 1723

and vegetables, inducing high thyroid exposures in people living in the affected areas (*2*).

So far, approximately 5,000 cases of radiation-induced thyroid cancer in children and adolescents have been diagnosed in those countries after the Chernobyl accident (*2*). Most of these cases have been treated and are being followed up in central institutions of the Ukraine (Institute of Endocrinology, Kiev) and Belarus (Center of Thyroid Tumors, Minsk). According to the data presented by Oliynik et al. (*3*) for the Ukraine and by Demidchik et al. (*4*) for Belarus, approximately 75% of the patients were between 10 and 15 y old at the time of their diagnosis. Up to 20% of the children presented with lung metastases. The only treatment available to cure these patients is radioiodine therapy with administered activities that are appropriate in metastatic differentiated childhood cancer (*5*). Thyroid cancer metastases usually take up radioiodine and are destroyed by high radiation-absorbed doses. Typically, 50 MBq/kg of body weight for ablation of thyroid remnants after thyroidectomy and 100 MBq/kg for subsequent treatment of distant metastases are administered (*4*). In most patients, the treatment had to be repeated several times. Radioiodine therapy proved to be effective because nearly all of the children and young adolescents treated with radioiodine responded to the therapy (*3–5*).

The article by Travis and Stabin (*1*) generally assesses the risk of breast cancer from $^{131}$I ablation treatment in young females; specific data on patients exposed to Chernobyl fallout are not included. The authors calculate that the radiation dose to pediatric or young adult female breast tissue associated with a 5.6-GBq ablation treatment ranges from 0.35 to 0.55 Gy, resulting in a lifetime risk of breast cancer ranging from 2 to 4 cases per 100 females exposed and a lifetime risk of solid tumors ranging from 8 to 17 solid tumors per 100 females exposed. Multiple treatment courses, as may be necessary in metastatic disease, could result in doses ranging from 0.7 to 1 Gy, with a corresponding increase in lifetime cancer risk. Using the body weight–adjusted $^{131}$I activities to be administered for ablation, the radiation dose estimates to breast tissue seem to be too high, particularly considering the fact that a considerable percentage of children without metastases shows complete remission after ablation therapy. However, often 5 or even more courses of radioiodine therapy were necessary to eliminate the lung metastases, resulting in cumulative radiation doses well above 1 Gy (*4*).

The dosimetric calculations in the study presented by Travis and Stabin (*1*) refer to whole-body data of $^{131}$I biokinetics in athyrotic patients. These data have not been derived from studies on children but were taken from published data on adults only. To confirm validity for children, it might be noted that radioiodine biokinetics were measured in Belarusian children and adolescents treated with $^{131}$I at the University of Würzburg, Germany (*4*). According to our data (*6*), effective whole-body half-life ranges from 0.5 to 0.6 d, which is shorter than the values used by Travis and Stabin.

Travis and Stabin (*1*) evaluate the literature with respect to major retrospective epidemiologic studies of women treated therapeutically with $^{131}$I and summarize that no increased risk for breast cancer after radioiodine therapy has been described (*1*). They suspect the reason for this observation to be that most women in these studies were over the age of 50 y at the time of exposure. Many younger women were included in a recent study not cited by Travis and Stabin (*7*). An increased incidence of breast cancer, compared with that of the general population, was found among women treated with radioiodine in the cohort of 6,841 thyroid cancer patients studied by Rubino et al. (*7*). This, however, was not related to $^{131}$I exposure, even among the women who were less than 40 y old at the time their thyroid cancer was diagnosed (*7*). On the other hand, Rubino et al. reported an increased risk of leukemia

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and solid tumors with increasing cumulative activities of $^{131}$I (bone and soft-tissue cancer, colorectal cancer, and salivary gland cancer). Adjadj at el. (*8*) investigated the risk of breast carcinoma after thyroid carcinoma in a separate group of French patients. Among 2,365 women who were treated for thyroid carcinoma, breast carcinoma subsequently developed in 48. Although a significant excess of breast cancer was observed among younger women, compared with women in the same age group in the general population, there was no significant correlation between relative risk and radiation dose to breast tissue (*8*). The risk tended to be lower for exposed patients than for patients without radiation exposure.

Recently, Chuang et al. (*9*) analyzed the United States Surveillance, Epidemiology and Results (SEER) database from 1973 to 2000 with respect to the risk of secondary cancers after treatment. Radiation therapy was associated with an increased risk that a second primary cancer would develop, the risk being higher for men and increasing with age. With respect to radioiodine therapy, no significantly increased breast cancer risk was observed in the cohort of 26,693 thyroid cancer patients; an increasing risk, however, was found for myeloid malignancies (*9*). Chuang et al. (*9*) claimed that their observation was related to the fact that they compared a radiation group with a nonradiation group among thyroid cancer patients, instead of using a less reliable comparison with the general population, as has been used in many other studies.

Interestingly, a recent analysis (*10*) of the complete data of the SEER registry (2,036,597 patients diagnosed with any type of cancer) revealed an association between thyroid cancer and leukemia or cancers of the breast, prostate, kidney, salivary glands, scrotum, and brain and central nervous system, irrespective of which cancer occurred first. Breast cancer contributed to 36% of all second cancers for female patients with thyroid cancer, accounting for a 0.2-fold elevated risk compared with the risk of the general U.S. population, with the risk being higher (1.42 vs. 1.15) in younger ($<$40 y) than in older ($\geq$40 y) patients. Of interest is the observation that the expected risk for female breast cancer in women treated with $^{131}$I for thyroid carcinoma (1.18) was not statistically significantly different from the risk in women without radiation treatment (1.25). For chronic lymphatic leukemia, however, a 2-fold increase in risk was shown after $^{131}$I therapy. The authors concluded that the 2-way positive associations between thyroid cancer and leukemia or cancers of the breast, prostate, kidney, salivary glands, brain and central nervous system, and scrotum suggest etiologic similarities and possible treatment effects.

In conclusion, presently, the only way to treat children and adolescents presenting with differentiated thyroid cancer after surgery is one or more courses of radioiodine therapy for remnant ablation and subsequent treatment of metastases. Most of the young patients from Belarus and Ukraine who have been treated so far have shown complete remission or, at least, stable disease (*4,5*).

According to Travis and Stabin (*1*), radioiodine therapy of thyroid cancer, particularly in young females with metastatic thyroid cancer, is associated with a comparatively high absorbed dose to breast tissue. According to published data on risk assessments, the risk for developing breast cancer is expected to increase after $^{131}$I therapy for thyroid cancer. Epidemiologic studies, however, failed to prove this hypothesis.

Because these risk assessments in very young patients are not well established, strategies for the lifetime follow-up and monitoring of the young Chernobyl victims should be developed and implemented, considering that breast cancer risk per se may increase in Belarus and Ukraine with time (*11*).

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