

Thyroid Stunning Revisited

In patients with thyroid carcinoma, remnant thyroid tissue or metastases may have lower ^{131}I uptake on posttherapy images than on prior diagnostic images. This observation has led to the hypothesis that radiation effects from the diagnostic dose may impair the ability of the remnant tissue or metastases to concentrate iodine, a process referred to as stunning. Some have recommended that diagnostic ^{131}I imaging doses should be limited to 74 MBq or less to decrease the likelihood of stunning. Others have recommended using ^{123}I for diagnostic imaging. ^{123}I has a low yield of conversion and Auger

EVIDENCE FOR AND AGAINST STUNNING

There is good evidence that stunning can happen, at least in remnant thyroid tissue. Most of the controversy involves the likelihood of stunning at specific ^{131}I doses and whether stunning causes any difference in therapeutic outcome.

A report 20 y ago by Jeevenram et al. (6) evaluated the effect of diagnostic radioiodine doses on subsequent uptake of ^{131}I ablative doses in 52 patients. The study found that the higher the estimated radiation-absorbed dose from the diagnostic ^{131}I , the greater the decrease in uptake of the therapy dose. No decrease in uptake was seen below an estimated radiation-absorbed dose of 17.5 Gy; however, there is considerable uncertainty in the radiation dose estimates. In a subset of 7 patients, 2 sequential ^{131}I doses of 148–185 MBq resulted in reductions of 40%–70% on the second uptake measurement in 6 of the 7 patients.

A retrospective study by Park et al. (7) is often cited as evidence of stunning. In this report, diagnostic and posttherapeutic scans were compared in 40 patients with thyroid carcinoma. A diagnostic imaging dose of 111–370 MBq of ^{131}I sodium iodide was used in 26 patients, and a dose of 11.1 MBq of ^{123}I was used in the remaining 14 patients. All patients received a therapy dose of 3,700–7,400 MBq of ^{131}I . The authors found a qualitative decrease in ^{131}I uptake in remnant thyroid tissue or metastases on posttherapy images in 20 of the 26 patients (77%); 15 of 24 neck foci (63%) but only 1 of 11 distant metastases (9%) exhibited the finding. The frequency of stunning increased with higher ^{131}I doses. No decrease in radioiodine uptake was found at any site in those who had received ^{123}I . Limitations of the study by Park et al.

include its retrospective nature, absence of quantitative data, and little distinction between remnant thyroid tissue and metastases in the neck.

Some qualitative studies have failed to confirm the presence of stunning. Cholewinski et al. (8) found no evidence of stunning in 122 patients (105 with thyroid remnant only, and 17 with metastases); in this study, 185 MBq of ^{131}I was used for imaging and 5,550 MBq for therapy. McDougall (9) studied 147 patients who received 74 MBq of ^{131}I for imaging and 1,110–7,400 MBq for therapy; posttreatment scans showed lower uptake in only 2 patients (1.4%).

Quantitative studies have shown variable results. Leger et al. (10) measured ^{123}I uptake in remnant thyroid tissue in 12 patients before a 185-MBq ^{131}I imaging dose and again before a therapy dose several weeks later. The second uptake value was significantly lower ($1.97\% \pm 0.71\%$ vs. initial value of $3.76\% \pm 1.50\%$; $P < 0.05$). In contrast, Dorn et al. (11) did not find evidence of stunning after a 370-MBq ^{131}I dose that was used for pretreatment dosimetry.

There is a model of impaired iodine transport at the cellular level after exposure of thyroid cells to ^{131}I . Postgård et al. (12) found that incubation with ^{131}I inhibits transepithelial transport of ^{125}I in cultured porcine thyroid cells and that the degree of inhibition is proportional to the radiation-absorbed dose.

CONTRIBUTION OF THE REPORT OF SISSON ET AL.

Quantitative ^{131}I uptake was compared on diagnostic and posttherapeutic ^{131}I scans at 48 h. Therapy doses were either 1,110 or 5,550 MBq of ^{131}I in all patients. In one group of 70 patients, diagnostic doses were 18.5,

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electrons, but it would not be expected to have a significant stunning effect.

Nearly everything about thyroid stunning has been controversial: whether it exists, whether there is a dose threshold, and whether it affects therapeutic outcome. There have been several recent reviews of the controversy (1–4). In this issue of *The Journal of Nuclear Medicine*, Sisson et al. (5) suggest that apparent stunning attributed to the diagnostic dose of ^{131}I may instead be an early effect of the therapy dose. Does their report mean that possible stunning from diagnostic ^{131}I doses, if it exists, can be ignored?

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37, and 74 MBq, a lower level than usually associated with stunning. Decreased uptake was seen on posttherapy images in 74%. In a second, prospective study of 10 patients who received 37-MBq diagnostic doses followed by therapy, posttherapy quantitative uptake measurements were obtained at additional time points, and uptake at 6–24 h was either measured or extrapolated from clearance data. In the second group, decreased ^{131}I uptake was seen at 48 h after therapy in 6 of the 10 patients, although in 5 of the 6 patients the estimated early uptake did not differ from the diagnostic study. The other 4 patients showed no substantial difference in uptake between diagnostic and therapeutic doses. The authors conclude that decreased ^{131}I activity after therapy in both groups is consistent with early destructive effects of the therapy dose and is not necessarily related to the diagnostic dose; this hypothesis is supported by the normal initial uptake of the therapy dose.

A limitation of the study of Sisson et al. (5) is the paucity of measured data within the first 2 d after the therapy dose. Lack of change in kinetics of early ^{131}I uptake would support the hypothesis of self-stunning by the therapy dose, but the initial uptake data in this study are mostly extrapolated. Another possible limitation is absence of data on camera response over the range of ^{131}I doses. ^{131}I uptake was determined from regions of interest on γ -camera images, but camera response may not be linear at high counting rates. The report states that patient studies showing observable dead time were excluded, but it is uncertain what measurements were acquired.

The findings in the study of Sisson et al. (5) are not altogether new. Hurley and Becker (13) found that the 24-h uptake of a therapy dose is usually lower than that of the scanning dose and that there is often rapid disappearance of ^{131}I from the thyroid after ablation. They concluded that the effects were presumably due to early radiation damage.

A major contribution of the report of Sisson et al. (5) is in calling attention to the possibility that many of the reported instances of stunning of thyroid remnants may represent effects of the therapy dose. It is likely that, at least in some cases, decreased retention of the ^{131}I therapy dose may be a favorable sign of therapeutic effect rather than evidence of stunning by the diagnostic dose.

POSSIBLE STUNNING OF METASTASES

Some reports on stunning do not distinguish between remnant normal thyroid tissue and metastases, and the results are skewed by the preponderance of remnant tissue. ^{131}I uptake in normal thyroid is almost always much greater than that in malignant thyroid tissue. Stunning of remnant tissue is plausible provided there is adequate ^{131}I uptake and remnant tissue mass. Achieving sufficient ^{131}I uptake in metastases to cause stunning is possible but much less likely. In one series of 83 cases of thyroid carcinoma in which ^{131}I uptake was measured after tumor excision, the highest uptake was 0.6% of the administered dose per gram of tumor; in most others, the uptake was less by an order of magnitude or more (14).

The sensitivity of ^{131}I imaging for metastases increases with increasing administered dose. Waxman et al. (15) showed greater sensitivity for a 370-MBq dose than for 74 MBq, and detection of metastases on a posttherapy scan but not the diagnostic scan is fairly common. Phantom studies (16) suggest that the sensitivity of ^{131}I imaging for small, deep metastases is surprisingly low, and decreasing the administered dose in an attempt to avoid stunning may be counterproductive. High-dose ^{123}I imaging is an alternative, albeit an expensive one, but there is not yet a consensus on optimum dose and imaging time.

CLINICAL IMPLICATIONS

The report of Sisson et al. (5) does not preclude the possibility that a di-

agnostic ^{131}I dose may cause stunning of remnant thyroid, as the authors clearly note. There are several possible ways to minimize the likelihood of stunning before ^{131}I ablation:

If the surgical history is known, and the ablative ^{131}I dose is based on risk factors for residual or metastatic thyroid cancer, imaging may not be needed before ablation.

If imaging is considered necessary before ablation, as some have argued (9), use of ^{123}I instead of ^{131}I will avoid stunning.

If ^{131}I imaging is performed before ablation, a 74-MBq dose is unlikely to cause significant stunning. A 185-MBq dose may cause stunning of remnant tissue, although satisfactory ablation is likely to be achieved anyway.

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