determined administered dose of RAI may be beneficial for patients with bone metastases (908), although this is not proven in controlled studies. Patients undergoing RAI therapy for bone metastases should also be considered for directed therapy of bone metastases that are visible on anatomical imaging (section [C38]). This may include surgery, external beam radiation therapy, and other focal treatment modalities. These patients should also be considered for systemic therapy with bone-directed agents (section [C47]).

[C31] When should empiric RAI therapy be considered for Tg-positive, RAI diagnostic scan–negative patients?

■ **RECOMMENDATION 80**

In the absence of structurally evident disease, patients with stimulated serum Tg <10 ng/mL with thyroid hormone withdrawal or <5 ng/mL with rhTSH (indeterminate response) can be followed without empiric RAI therapy on continued thyroid hormone therapy alone, reserving additional therapies for those with rising serum Tg levels over time or other evidence of structural disease progression.

(Weak recommendation, Low-quality evidence)

■ **RECOMMENDATION 81**

Empiric (100–200 mCi) or dosimetrically determined RAI therapy may be considered in patients with more significantly elevated serum Tg levels (see Recommendation 80), rapidly rising serum Tg levels, or rising ant-Tg antibody levels, in whom imaging (anatomic neck/chest imaging and/or ^{18}FDG-PET/CT) has failed to reveal a tumor source that is amenable to directed therapy. The risk of high cumulative administered activities of RAI must be balanced against uncertain long-term benefits. If empiric RAI therapy is given and the posttherapy scan is negative, the patient should be considered to have RAI-refractory disease and no further RAI therapy should be administered.

(Weak recommendation, Low-quality evidence)

■ **RECOMMENDATION 82**

If persistent nonresectable disease is localized after an empiric dose of RAI, and there is objective evidence of significant tumor reduction, then consideration can be made for RAI therapy to be repeated until the tumor has been eradicated or the tumor no longer responds to treatment. The risk of repeated therapeutic doses of RAI must be balanced against uncertain long-term benefits.

(Weak recommendation, Low-quality evidence)

Factors to consider when selecting patients for empiric RAI therapy include the level of serum Tg elevation and the results of ^{18}FDG-PET scanning, if performed. Since tumors that are ^{18}FDG-PET positive generally do not concentrate RAI (965), RAI therapy is much less likely to be efficacious (965,966) and it is unlikely to alter the poorer outcome in such patients (823). Because of this, it is reasonable to perform ^{18}FDG-PET/CT scanning prior to consideration of empiric RAI therapy (967).

The cutoff value of serum Tg above which a patient should be treated with an empiric dose of RAI is not clear. Most studies have reported primarily on patients with Tg levels after T_4 withdrawal of 10 ng/mL or higher; it has been suggested that a corresponding level after rhTSH stimulation would be 5 ng/mL (321,782,962,968,969). Patients with a suppressed (624) or stimulated (970) serum Tg of 5 ng/mL or higher are unlikely to demonstrate a decline without therapy, and they have higher rates of subsequent structural recurrence than those with lower serum Tg levels (970). In addition, a rising serum Tg indicates disease that is likely to become clinically apparent, particularly if it is rapidly rising (622,971,972).

If serum Tg levels suggest residual or recurrent disease, but diagnostic RAI WBS imaging is negative and structural imaging does not reveal disease that is amenable to directed therapy (surgical, thermal ablation, EBRT, alcohol ablation, see section [C17 and C38]), then empiric therapy with RAI (100–200 mCi) or dosimetrically determined RAI activities can be considered for two purposes: (i) to aid in disease localization, and/or (ii) as therapy for nonsurgical disease. This approach may identify the location of persistent disease in approximately 50% of patients (968,973,974), although the reported range of success is wide. From a therapeutic perspective, over half of patients experience a fall in serum Tg after empiric RAI therapy in patients with negative diagnostic WBS (963,969,975,976); however, there is no evidence for improved survival with empiric therapy in this setting (782,962,968). Further, there is evidence that Tg levels may decline without specific therapy in a significant proportion of patients with Tg levels <10 ng/mL (539,618–620,624,782,970–972,975,977–979). The most compelling evidence for benefit from empiric RAI therapy is for pulmonary metastases, which are not amenable to surgical management or EBRT (782,844,980).

[C32] What is the management of complications of RAI therapy?

■ **RECOMMENDATION 83**

The evidence is insufficient to recommend for or against the routine use of measures to prevent salivary gland damage after RAI therapy.

(No recommendation, Low-quality evidence)

■ **RECOMMENDATION 84**

Patients with xerostomia are at increased risk of dental caries and should discuss preventive strategies with their dental/oral health professional.

(Weak recommendation, Low-quality evidence)

■ **RECOMMENDATION 85**

Surgical correction should be considered for nasolacrimal outflow obstruction, which often presents as excessive tearing (epiphora) but also predisposes to infection.

(Strong recommendation, Low-quality evidence)

While RAI appears to be a reasonably safe therapy, it is associated with a cumulative dose-related low risk of early- and late-onset complications such as salivary gland damage, dental caries (981), nasolacrimal duct obstruction (982), and secondary malignancies (762,763,961,983,984), and it may likely contribute to long-term dysphagia (985). Therefore, it is important to ensure that the benefits of RAI therapy, especially repeated courses, outweigh the potential risks. There is probably no dose