Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

Differentiated thyroid cancer: management of localized disease

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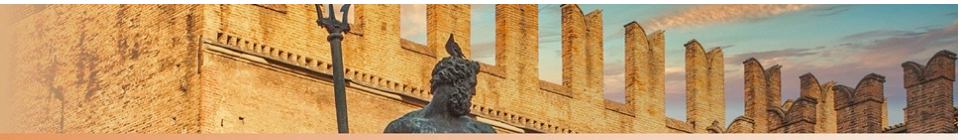


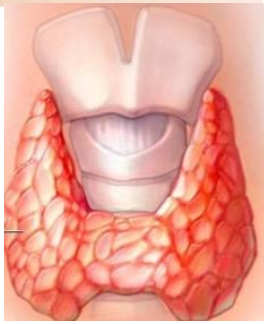
DICHIARAZIONE

Relatore: SARA TALOMO

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Consulenza ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazione ad Advisory Board NIENTE DA DICHIARARE
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE

Goals of Treatment of Differentiated Thyroid Cancer (DTC)



- to remove the primary tumor
- to minimize the risk of recurrence

ATTENTION!

QoL
Late Toxicity

- Operable Disease
- Persistence of disease after initial treatment
- Inoperable Disease

- Operable Disease
- Persistence of disease after initial treatment
- Inoperable Disease

Operable disease

SURVEILLANCE

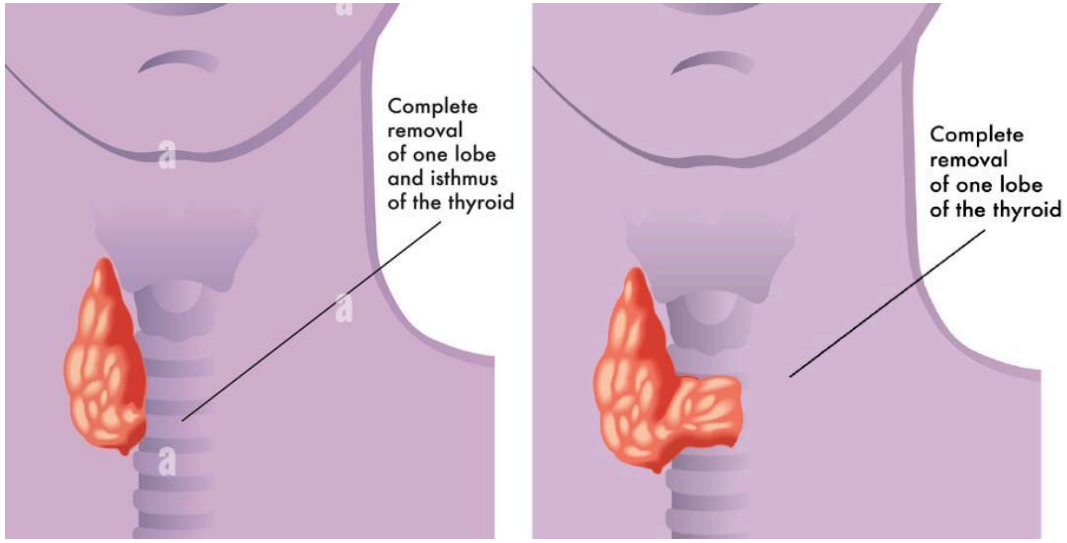
- unifocal papillary microcarcinomas (<10 mm)
- no evidence of extracapsular extension
- no evidence of lymph node metastases
- no risk factors in anamnesis
- no aggressive features in citology
- surgical risks
- consider age

Active US Surveillance

Ito Y Eur J Surg Oncol 2018; Miyauchi Surgery 2018

Operable disease

HEMITHYROIDECTOMY OR LOBECTOMY



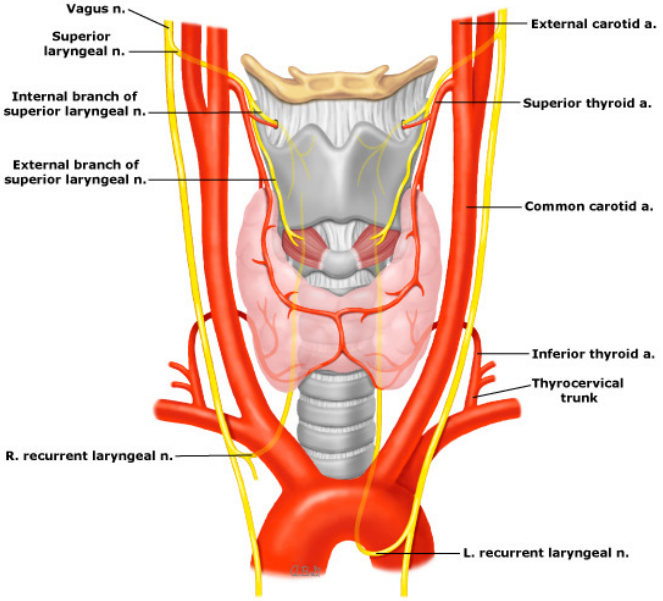
Proposed for

- T1a – T2, N0
- Close to trachea, posterior or adjacent

Adam *Ann Surg* 2014; Hauch *Ann Surg Oncol* 2014

Operable disease

TOTAL THYROIDECTOMY (STILL STANDARD?)



- Risk of Post-operative Complications? → number of interventions
- Lower Risk of Recurrence
- Possibility to use radioactive iodine (RAI) therapy

RAI post Total Thyroidectomy

Over the past years, RAI was indicated in almost every patient with DTC

... revision of patients' outcome has introduced the concept of *risk-based selection* candidates to RAI ablation.

Individual risk depends upon:

- initial prognostic indicators at surgery
- neck ultrasonography after surgery
- serum tireoglobuline (Tg) measurements

According to these parameters, ATA has defined *three groups* of patients with different risks of recurrence and the benefits of postoperative 131I differ among these groups

RAI post Total Thyroidectomy

Risk of disease persistence or recurrence

RECOMMENDATION 51

- RAI adjuvant therapy is **routinely recommended** after total thyroidectomy for ATA high risk DTC patients (Strong recommendation, Moderate-quality evidence)

- RAI adjuvant therapy **should be considered** after total thyroidectomy in ATA intermediate-risk level DTC patients. (Weak recommendation, Low-quality evidence)

- RAI remnant ablation **is not routinely recommended** after thyroidectomy for ATA low-risk DTC patients. Consideration of specific features of the individual patient that could modulate recurrence risk, disease follow-up implications, and patient preferences are relevant to RAI decision-making. (Weak recommendation, Low-quality evidence)

Haugen *Thyroid* 2016

RAI post Total Thyroidectomy

Eur J Nucl Med Mol Imaging (2016) 43:1001–1005
DOI 10.1007/s00259-016-3327-3

EDITORIAL

Why the European Association of Nuclear Medici to endorse the 2015 American Thyroid Associatio guidelines for adult patients with thyroid nodules and differentiated thyroid cancer

Frederik A. Verburg[1] · Cumali Aktolun[2] · Arturo Chiti[3,4] · Savvas Frangos[5] · Luca Giovanella[6] · Martha Hoffmann[7] · Ioannis Iakovou[8] · Jasna Mihailovic[9] · Bernd J. Krause[10] · Werner Langsteger[11] · Markus Luster[12] · on behalf of the EANM and the EANM Thyroid Committee

Eur J Nucl Med Mol Imaging (2017) 44:918–925
DOI 10.1007/s00259-017-3654-z

EDITORIAL

Radioiodine treatment after surgery for differentiated thyroid cancer: a reasonable option

Jérôme Clerc[1] · Frederik A. Verburg[2] · Anca M. Avram[3] · Luca Giovanella[4] · Elif Hindié[5] · David Taïeb[6]

Endorsement

Eur J Nucl Med Mol Imaging (2017) 44:183–184
DOI 10.1007/s00259-016-3526-y

rative I-131 therapy in differentiated thyroid 2015 ATA guidelines an exact science or a dark

Luster[1] · Luca Giovanella[2]

"...in DTC the data in the literature are so limited that a real evidence-based discussion is almost impossible and any one experience-based opinion may carry as much weight as another"

RAI post Total Thyroidectomy

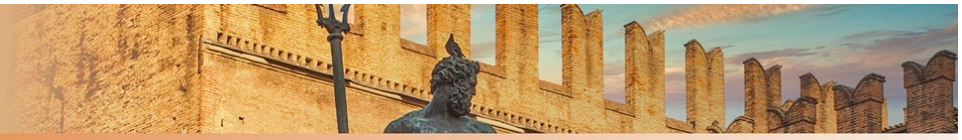
European Thyroid JOURNAL | F Pacini *et al.* | DTC radioiodine treatment Consensus Statement | 11:1 | e210046

CONSENSUS STATEMENT

2022 ETA Consensus Statement: What are the indications for post-surgical radioiodine therapy in differentiated thyroid cancer?

Furio Pacini[1], Dagmar Fuhrer[2], Rossella Elisei[3], Daria Handkiewicz-Junak[4], Sophie Leboulleux[5], Markus Luster[6], Martin Schlumberger[5] and Johannes W Smit[7]

- The use of I-131 therapy as adjuvant treatment or treatment of known disease **is indicated** for patients in the high risk of recurrence category or with known structural disease
- In the intermediate-risk category, RAI therapy **may be indicated** and should be tailored according to individual cases.
- In low-risk patients, the benefit of I-131 therapy is a matter of intensive scientific debate and the decision on whether to perform RAI therapy should be based on the **presence of individual risk modifiers.**



- Operable Disease
- Persistence of disease after initial treatment
- Inoperable Disease

Persistence of disease after initial treatment

Biochemical incomplete response	Negative imaging but presence of serum Tg
Indeterminate response	Nonspecific biochemical and structural findings
Structural incomplete response	Imaging evidence of disease

Biochemical disease

Loco-regional or oligometastatic

⇩

Metastatic disease

OPZIONI TERAPEUTICHE

- ✓ TSH suppression
- ✓ Surgery if possible
- ✓ ^{131}I if responder disease
- ✓ External beam RT/other locoregional treatment
- ✓ TKI

Persistence of disease after initial treatment

External beam radiotherapy (EBRT)

ATA 2016: does not advise the use of adjuvant EBRT to the neck except in the case of multiple neck recurrences

NCCN: EBRT should be considered for unresectable disease or gross residual tumor after surgical resection

Adjuvant RT for high-risk disease (after R1 resection)

- Microscopic disease (thyroid bed, involved resected lymph node regions): 60–66 Gy in 1.8–2 Gy per fraction
- Elective nodal regions: 50–56 Gy in 1.6–2 Gy per fraction

Salvage EBRT after R2 resection or inoperable patients

- Gross disease: 66–70 Gy in 1.8–2 Gy per fraction
- Microscopic disease (thyroid bed, involved resected lymph node regions): 60–66 Gy in 1.8–2 Gy per fraction
- Elective nodal regions: 50–56 Gy in 1.6–2 Gy per fraction

AIRO: EBRT should be considered for pT4a/T4b if >45yo, gross residual disease, recurrence disease that failed to concentrate RAI

Haugen *Thyroid* 2016; NCCN Guidelines2022; Mangoni *Tumori* 2017;

Persistence of disease after initial treatment

External beam radiotherapy (EBRT)

Adjuvant RT for high-risk disease (after R1 resection)

- Microscopic disease (thyroid bed, involved resected lymph node regions): 60–66 Gy in 1.8–2 Gy per fraction
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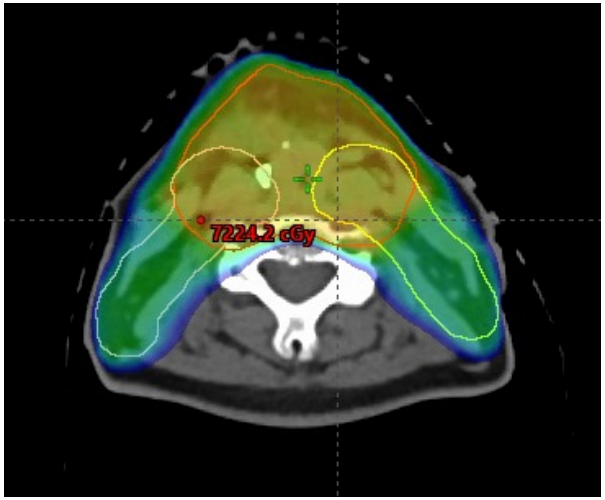
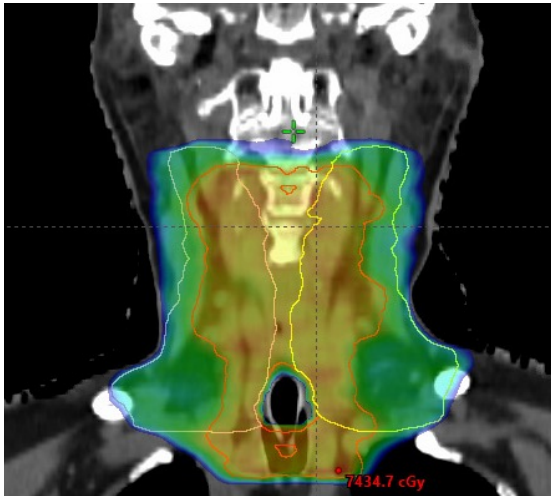




Persistence of disease after initial treatment

EBRT

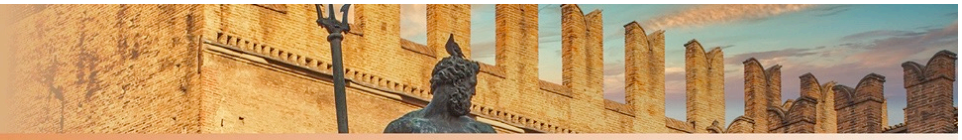
Well-Differentiated Thyroid Cancer: Who Should Get Postoperative Radiation?

Dauren Adilbay, MD, PhD[1], Avery Yuan, MB[1], Paul B. Romesser, MD[2,3], Richard J. Wong, MD[1], Jatin P. Shah, MD[1], Ashok R. Shaha, MD[1], Michael R. Tuttle, MD[4], Snehal Patel, MD[1], Nancy Y. Lee, MD[2], and Ian Ganly, MD[1]

Selected patients who received EBRT had improved Locoregional recurrent-free probability, however this did not translate into improved DSS and OS.

Recommendation: use of EBRT only in selected patients with locally advanced primary tumors who are deemed to have high risk of central neck recurrence for which salvage surgery would result in an unacceptable risk to airway.

Ann Surg Oncol 2022



- Operable Disease
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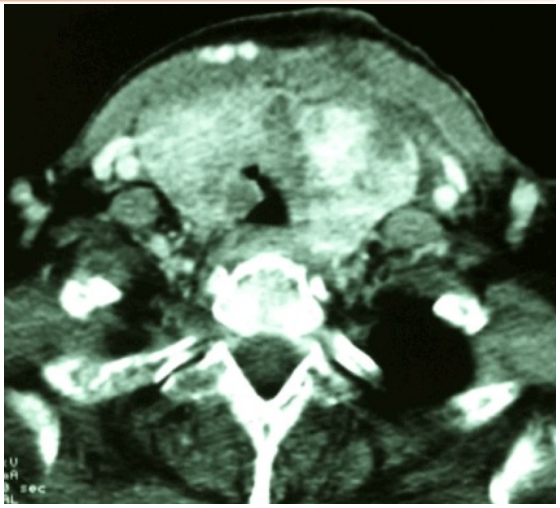
Inoperable disease



Surgery: Objective of debulking or removing gross tumor

Often direct tumor extension to surrounding organs:

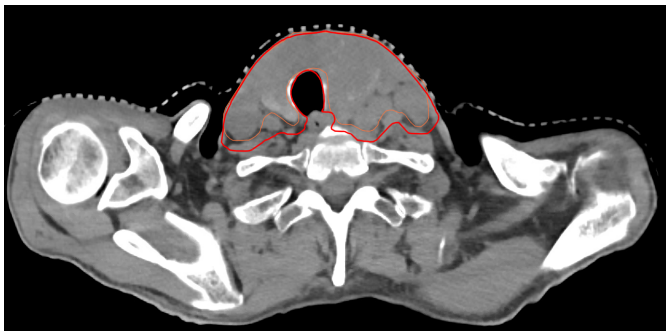
- recurrent laryngeal nerve
- larynx
- trachea
- esophagus

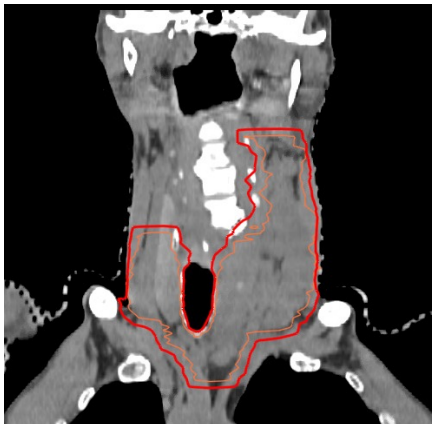
QoL
Late Toxicity

Inoperable disease

EBRT:

- Gross disease: 66–70 Gy in 1.8–2 Gy per fraction
- Elective nodal regions: 50–56 Gy in 1.6–2 Gy per fraction





Inoperable disease

Tyrosine kinase inhibitors (TKI)

- Imminently threatening disease progression expected to require intervention and/or to produce morbidity or mortality in <6 months

e.g., lymphadenopathy likely to rapidly invade airways, produce dyspnea, or cause bronchial obstruction

- Symptomatic disease

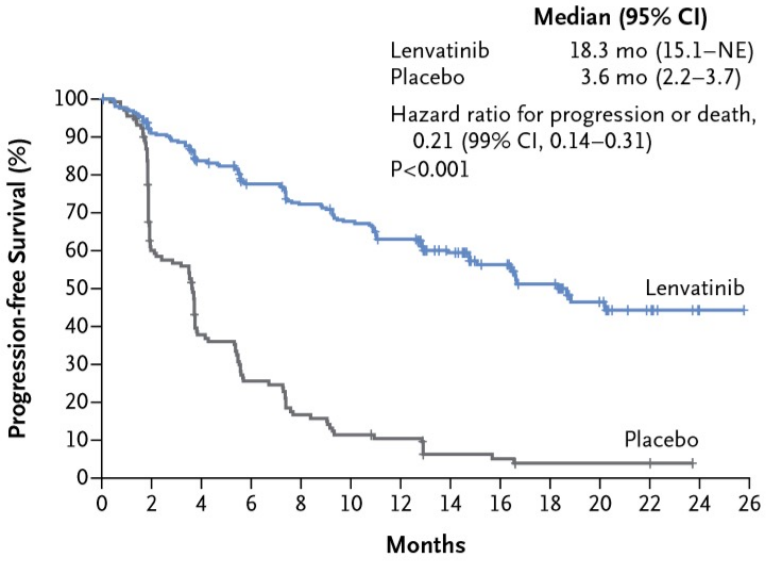
e.g., exertional dyspnea, painful unresectable adenopathy, not adequately addressable using directed therapy.

Inoperable disease

Fascia C

1st line:

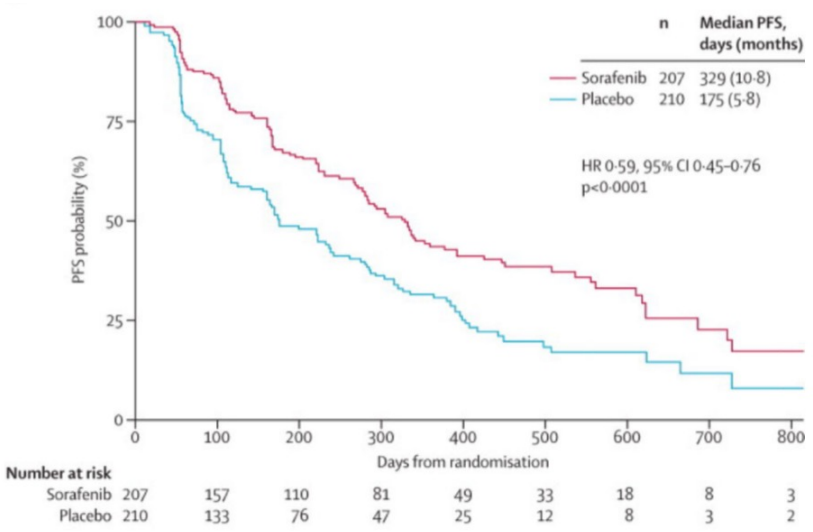
- Levatinib is an inhibitor of VEGFR, FGFR, RET, c-KIT, and PDGFR



NEJM 2015

1st line

- Sorafenib is a multikinase inhibitor that targets VEGFR, PDGFR, FGFR, c-KIT, BRAF, and RET



Lancet 2014

Differentiated thyroid cancer has an excellent prognosis in both pediatric and adult populations. Few patients will present a progressive disease, radioiodine refractory and requiring closer attention and additional therapy.

Surgery, EBRT and TKI may be important options in patients with progressive local disease

A multidisciplinary team is essential for management of the aggressive presentation of DTC

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