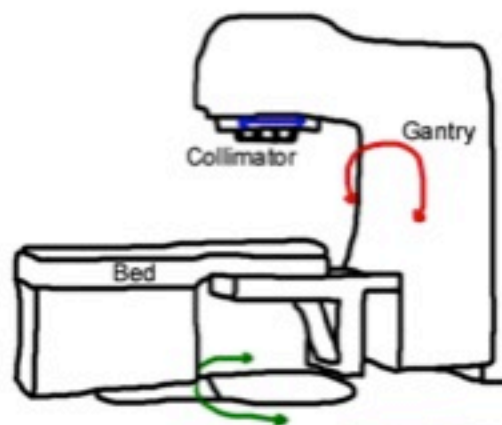


Il carcinoma tiroideo in progressione: la radioterapia

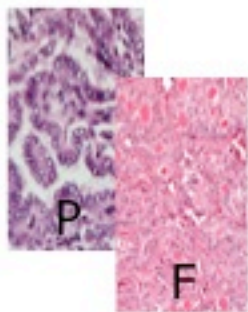
G Minniti



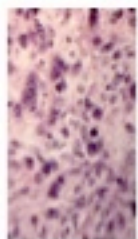
Radiation Oncology Unit



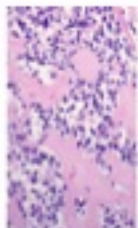
➤ *Carcinoma della tiroide*



Differenziato



Anaplastico



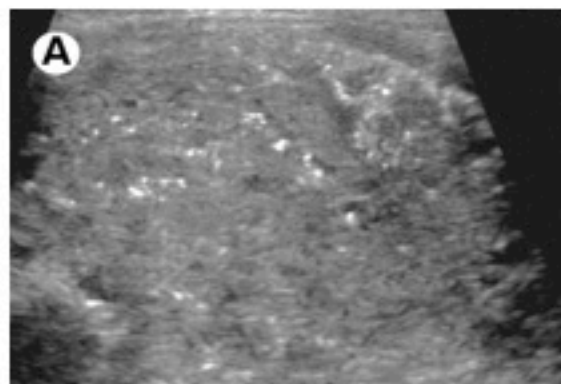
Midollare



Carcinoma della Tiroide

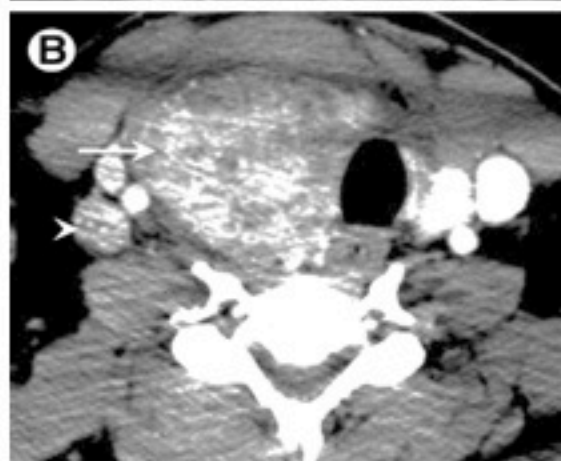
TNM CLASSIFICATION SYSTEM FOR DIFFERENTIATED THYROID CARCINOMA

T1	Tumor diameter 2 cm or smaller
T2	Primary tumor diameter >2 to 4 cm
T3	Primary tumor diameter >4 cm limited to the thyroid or with minimal extrathyroidal extension
T4 _a	Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve
T4 _b	Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels
TX	Primary tumor size unknown, but without extrathyroidal invasion
N0	No metastatic nodes
N1 _a	Metastases to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)
N1 _b	Metastasis to unilateral, bilateral, contralateral cervical or superior mediastinal nodes
NX	Nodes not assessed at surgery
M0	No distant metastases
M1	Distant metastases
MX	Distant metastases not assessed



➤ T4a disease

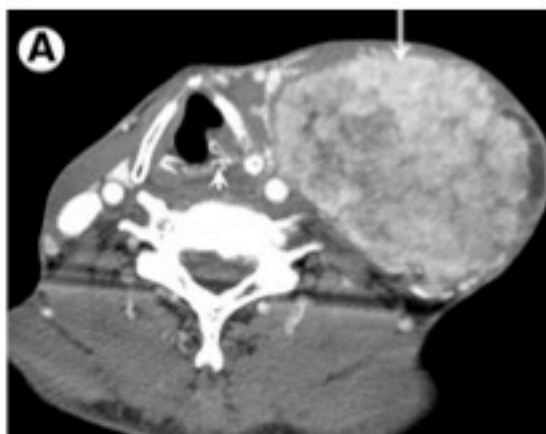
(A) Longitudinal US view of the right thyroid demonstrates large heterogeneous mass with microcalcifications (measured at 6 cm). No abnormal nodes were reported.



(B) Axial CT again demonstrates the right thyroid mass (arrow). Moreover, it shows an abnormal right level IV lymph node (arrowhead), which would necessitate a lateral neck dissection.

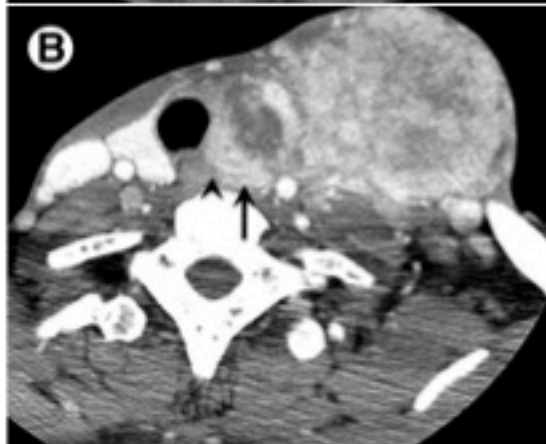


(C) Axial CT more inferiorly shows a metastatic superior mediastinal lymph node (arrow), also not detected on US.

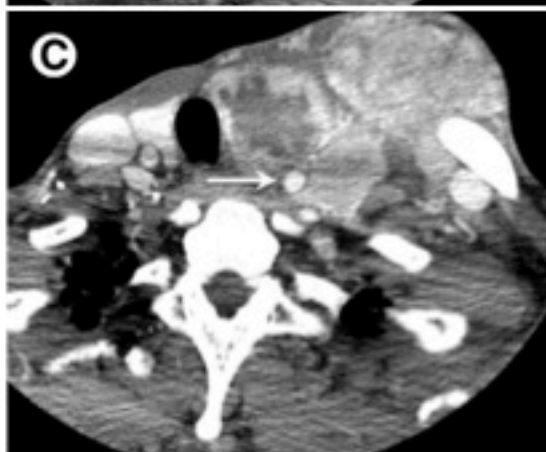


➤ *T4b disease*

(A) Axial CT at the level of the true vocal cord demonstrates left true vocal cord paralysis (arrowhead) and a large left neck conglomerate nodal mass (arrow).

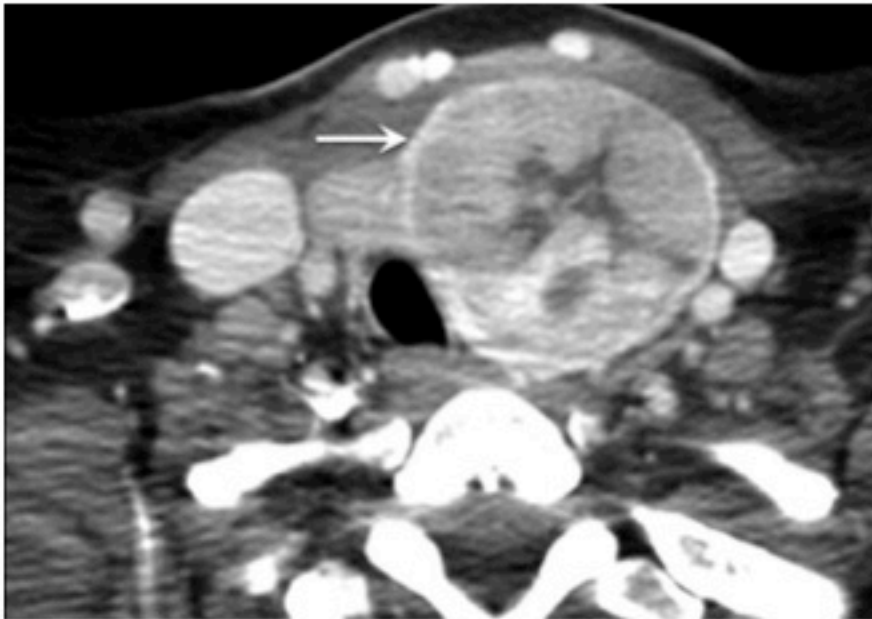


(B) Axial CT at the level of the thyroid demonstrates a heterogeneous mass in the left thyroid lobe extending posteriorly to the prevertebral musculature (arrow) with indistinct margins with the esophagus (arrowhead).



(C) Axial CT shows encasement of the common carotid artery by a combination of the primary tumor and conglomerate lymphadenopathy (arrow). These findings would upstage to **T4b**. At surgery, tumor was found to be grossly invading the larynx, esophagus, and prevertebral fascia.

Stage T3 follicular carcinoma



Axial CT shows a well circumscribed solid 4.8-cm mass in the left thyroid lobe (arrow). Surgical pathology showed a follicular carcinoma.

Carcinoma della Tiroide: forme differenziate

Carcinomi differenziati

“Low risk”



Età < 45 aa

M0

T1/T2 (<4cm)

Istotipo (ca papillare)

Carcinomi differenziati

“High risk”



Età > 45 aa

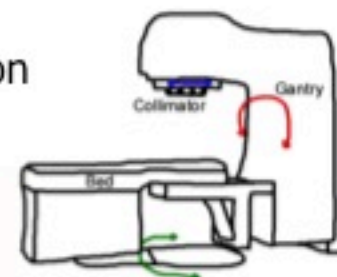
M+

T3/T4 (>4cm)

Istotipo (ca follicolare o varianti aggressive ca papillare)

Carcinoma della tiroide differenziato

Guidelines for the management of thyroid cancer - British Thyroid Association



Adjuvant external beam radiotherapy

The main indications for adjuvant radiotherapy are:

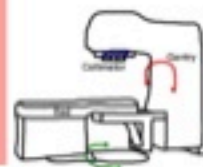
- i gross evidence of local tumour invasion at surgery, presumed to have significant macro- or microscopic residual disease, particularly if the residual tumour fails to concentrate sufficient amounts of radioiodine
- ii extensive pT4 disease in patients over 60 years of age with extensive extranodal spread after optimal surgery, even in the absence of evident residual disease.

High-dose external beam radiotherapy as part of primary treatment*

High-dose external beam radiotherapy is indicated for (IV, C):

- i unresectable tumours that do not concentrate radioactive iodine
- ii unresectable bulky tumours in addition to radioactive iodine treatment.

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer



The use of external beam irradiation to treat the primary tumor should be considered in patients over age 45 with grossly visible extrathyroidal extension at the time of surgery and a high likelihood of microscopic residual disease, and for those patients with gross residual tumor in whom further surgery or RAI would likely be ineffective. The sequence of external beam irradiation and RAI therapy depends on the volume of gross residual disease and the likelihood of the tumor being RAI responsive. Recommendation rating: B

External Beam Radiation Therapy for Thyroid Cancer

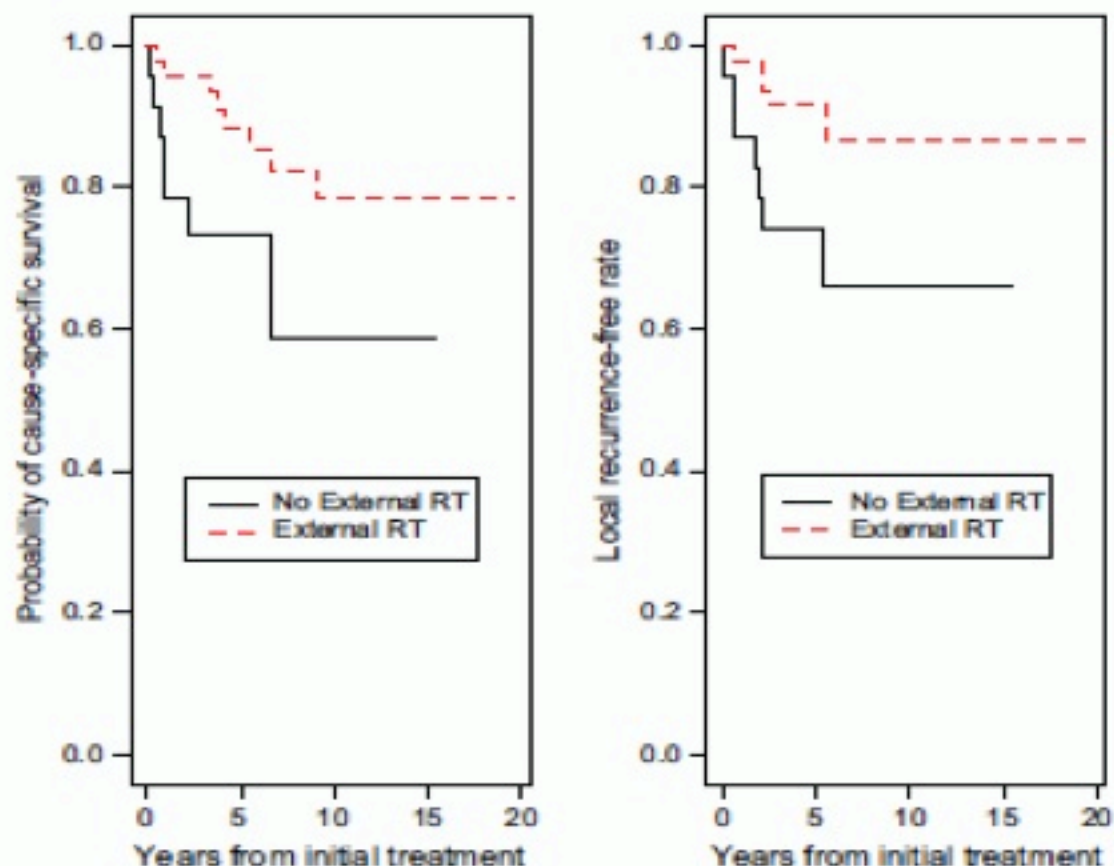
Ten-year local recurrence rates after adjuvant external radiation therapy for high-risk disease

Study	Treatment	
	Surgery with RAI (%)	Surgery, RAI, and XRT (%)
Tubiana et al [15]	21	14
Simpson et al [53]	18	14
Phlips et al [54]	21	3
Farahati et al [9] (includes distant failures)	50	10
Tsang et al [7] (papillary only)	22	7
Kim et al [55] (papillary only, 5 year rates)	37.5	4.8
Keum et al [56]	89	38
Brierley et al [20] (patients over 60 who have ETE)	34.3	13.6
Chow et al [14] (papillary only with T4a)	17.6	11.6

Prognostic factors and the effect of treatment with radioactive iodine and external beam radiation on patients with differentiated thyroid cancer seen at a single institution over 40 years

J. Brierley*†, R. Tsang*†, T. Panzarelli‡§ and N. Bana*

*Department of Radiation Oncology, Princess Margaret Hospital, Toronto, †Department of Radiation Oncology, University of Toronto, ‡Department of Biostatistics, Princess Margaret Hospital, University of Toronto and §Department of Public Health Sciences, University of Toronto, Toronto, Ontario, Canada



- Nei pz ad alto rischio di recidiva la EBRT aumenta l'intervallo libero da malattia e la sopravvivenza cancro-specifica

Local and regional control in patients with papillary thyroid carcinoma: specific indications of external radiotherapy and radioactive iodine according to T and N categories in AJCC 6th edition

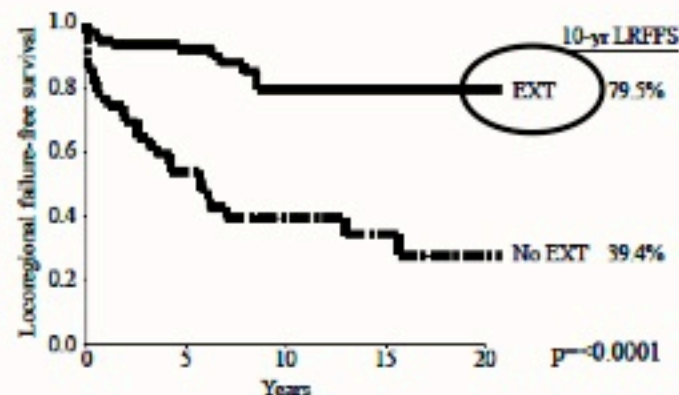


Figure 1 Locoregional failure-free survival in patients with gross but non-palpable residual disease: role of EXT (n=137).

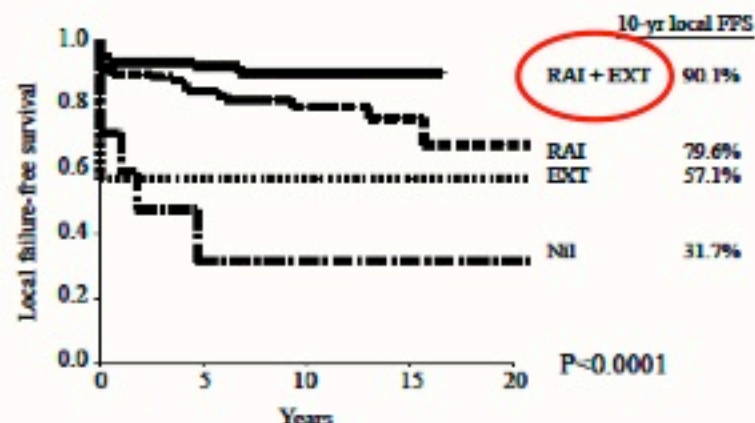


Figure 2 Local failure-free survival in patients with 'positive' resection margins after total thyroidectomy: role of RAI and EXT

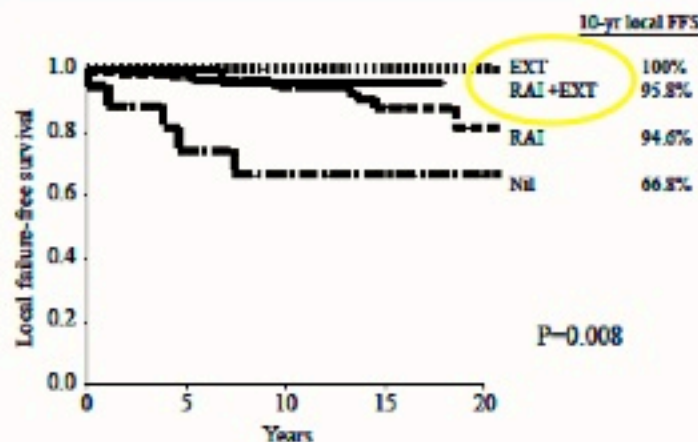


Figure 3 Local failure-free survival in T3b disease after total thyroidectomy: role of RAI and EXT (n=352).

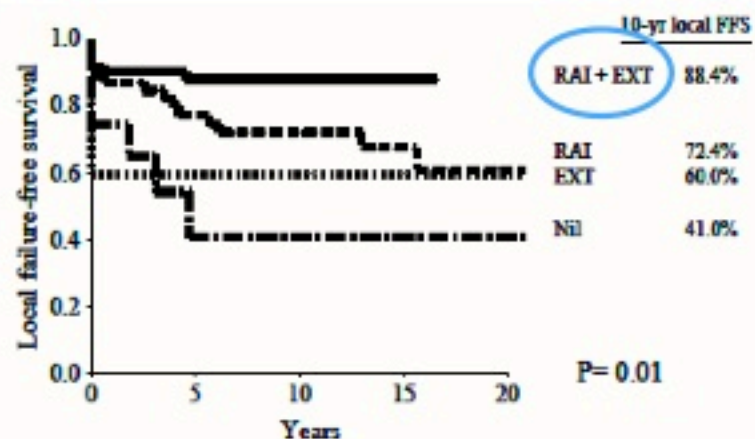


Figure 4 Local failure-free survival in T4a disease after total thyroidectomy: role of RAI and EXT (n=131).

Local and regional control in patients with papillary thyroid carcinoma: specific indications of external radiotherapy and radioactive iodine according to T and N categories in AJCC 6th edition

Conclusioni

La Radioterapia è indicata:

- *Pz con residuo macroscopico post-operatorio*
- *Margini di resezione positivi*
- *Malattia T4*
- *Linfonodi N1b o linfonodi > 2 cm*

Tecnica radioterapica

➤ Planning Target Volume

- ✓ Regione tiroidea ed il collo fino alle mastoidi ed all'osso ioide
- ✓ Regioni sopraclaveari
- ✓ Mediastino superiore fino alla carena
- ✓ 50-60 Gy 5fr./W 1.8-2.0 Gy
- ✓ Eventuale boost 6-10 Gy con e-

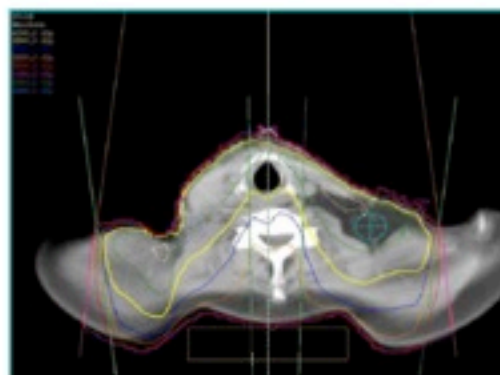
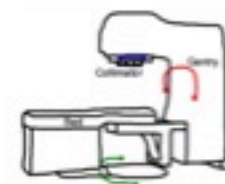
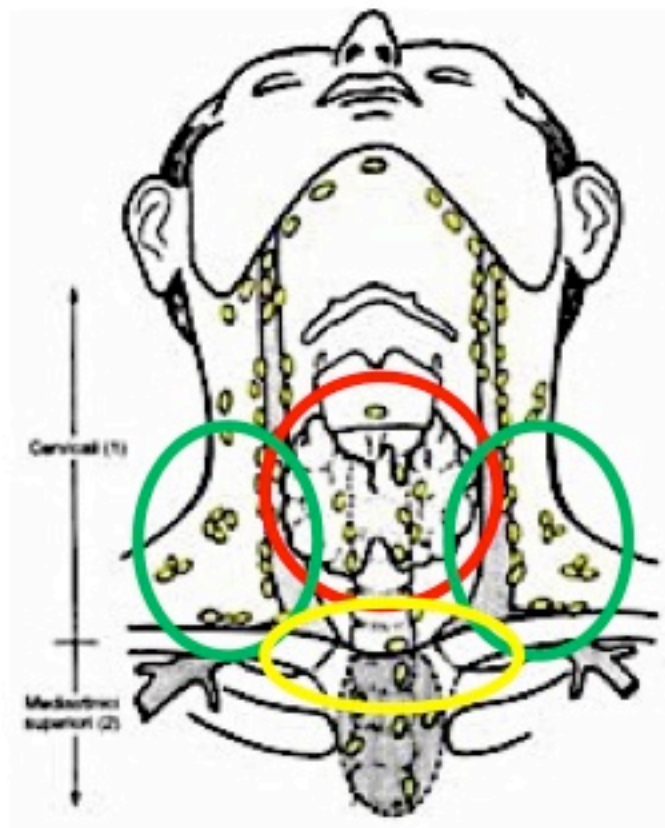


Fig. 2. Anterior-posterior parallel opposed pair with dominant anterior weighting beam. Spinal cord shielding was introduced in the last 4 fractions of radiotherapy.

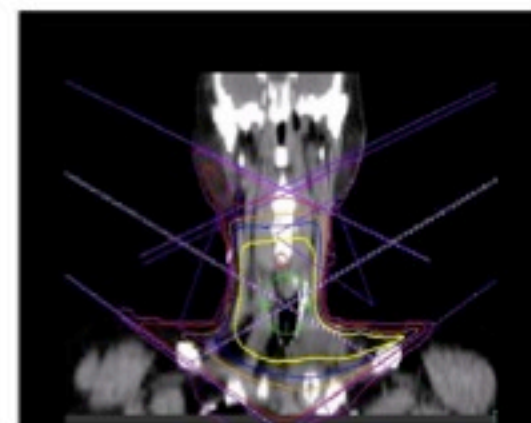
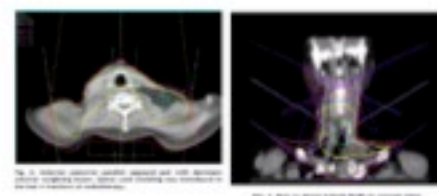


Fig. 1. Non co-planar lateral fields in coronal plane.

Patterns of relapse following radiotherapy for differentiated thyroid cancer: Implication for target volume delineation



Summary of studies illustrating improvement in locoregional control rates with EBRT for thyroid cancer

Author	EBRT n	Local control with EBRT (%)		No EBRT n	Local control without EBRT(%)	
		5 yr	10 yr		5 yr	10 yr
Tubiana [3]	180		86	336		79
Tsang [11]	90		93	65		78
Farahati [10]	99		90	70		56
Chow [15]	69		64	55		29
Philips [7]	38	97		56	79	
Kim [16]	23	95		68	67.5	
Our study	49	81.4				

Summary of studies showing the local control rates in patients with gross or macroscopic disease treated with radioiodine and EBRT using different dose and fractionation

Author	Number of patients n	Dose (Gy)/total fractions #/ overall treatment time (days)	Dose per fraction(Gy)	BED (Gy)		5-year Local control
				$\alpha/\beta = 1.5$	$\alpha/\beta = 10$	
Tsang [11]	33	50Gy/20#/28	2.5	133	62.0	62.0%
Chow [15]	69	60Gy/30#/42	2.0	140	72.0	67.0%
Our study	19	47.5Gy/16#/22	2.97	141	61.6	69.2%

Biological equivalent dose BED = $nd(1 + [d/(\alpha/\beta)])$.

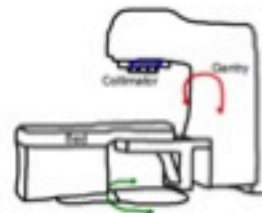
n = number of fractions, d = fraction size.

The Management of Advanced Thyroid Cancer

P. C. Wilson*, B. M. Millar†, J. D. Brierley†

*Department of Clinical Oncology, Bristol Haematology and Oncology Centre, Bristol, UK;

†Department of Radiation Oncology, Princess Margaret Hospital, Toronto, Ontario, Canada

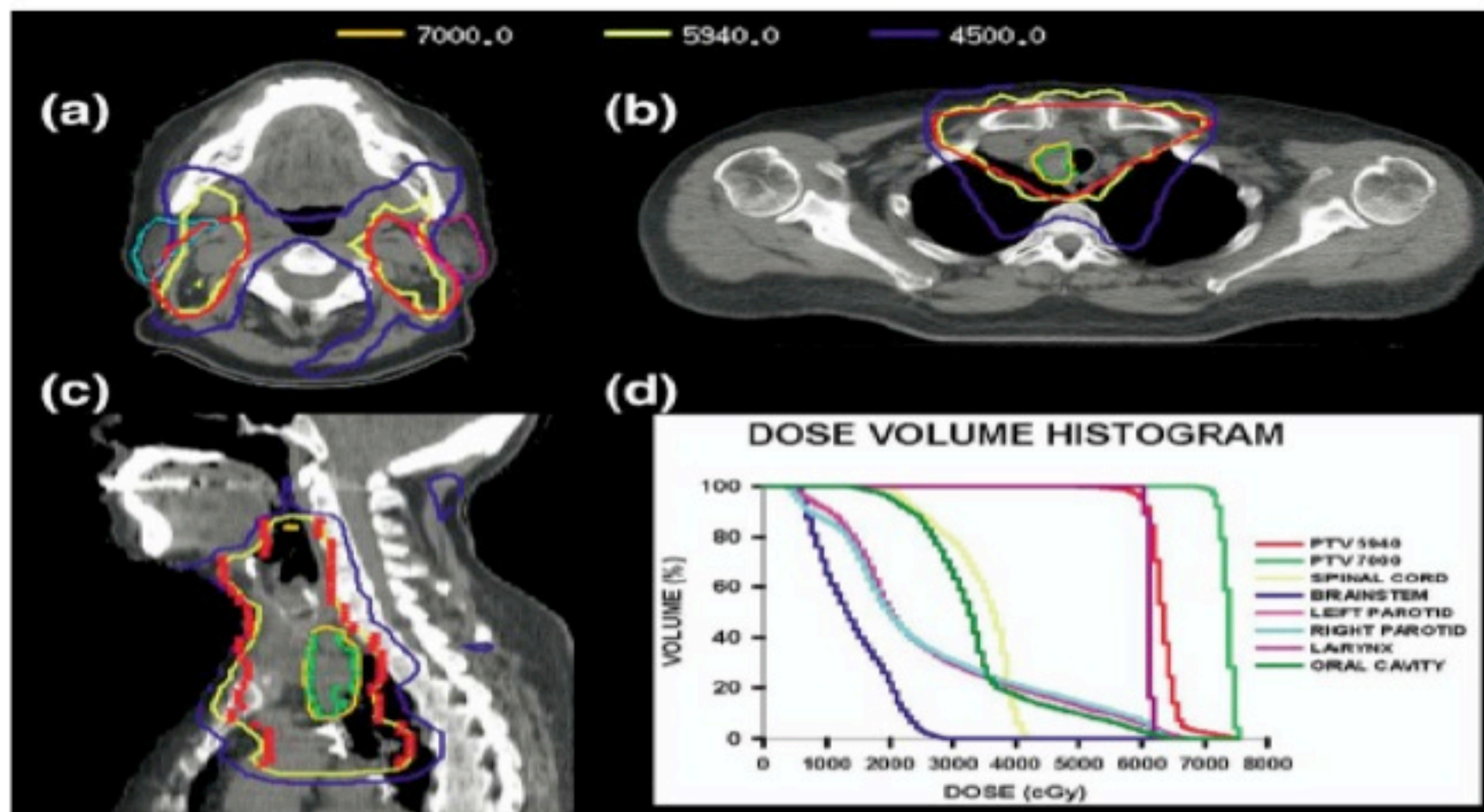


Linee guida della “British Thyroid Association and the Royal College of Physicians” per le dosi dell’ EBRT

- *50 Gy in 20 fr se grosso residuo*
- *40 Gy in 15 fr. se residuo microscopico*
- *Se vengono trattati anche i linfonodi sovraclaveari (grandi volumi), o in presenza di estensione extracapsulare il frazionamento di scelta è di 200cGy a frazione*

INTENSITY-MODULATED RADIATION THERAPY FOR THE TREATMENT OF NONANAPLASTIC THYROID CANCER

BENJAMIN D. ROSENBLUTH, M.D.,* VICTORIA SERRANO, B.S.,* LAURA HAPPERSETT, M.S., M.A.,†
 ASHOK R. SHAHA, M.D.,‡ R. MICHAEL TUTTLE, M.D.,§ ASHWATHA NARAYANA, M.D.,*
 SUZANNE L. WOLDEN, M.D.,* KENNETH E. ROSENZWEIG, M.D.,* LANCEFORD M. CHONG, M.D.,*
 AND NANCY Y. LEE, M.D.*



Intensity Modulated Radiotherapy (IMRT) in locally advanced thyroid cancer: Acute toxicity results of a phase I study

Teresa Guerrero Urbano^{a,c}, Catharine H. Clark^{b,d}, Vibeke N. Hansen^{b,d}, Elizabeth J. Adams^{b,d}, Elizabeth A. Miles^{b,d}, Helen Mc Nair^{b,d}, A. Margaret Bidmead^{b,d}, Jim Warrington^{b,d}, David P. Dearnaley^{b,c}, Clive Harmer^a, Kevin J. Harrington^{a,c}, Christopher M. Nutting^{a,*}

^aHead and Neck Unit, and ^bDepartment of Radiotherapy, Royal Marsden Hospital, London, UK, ^cThe Institute of Cancer Research, London, UK, ^dDepartment of Physics, Royal Marsden Hospital, Surrey, UK

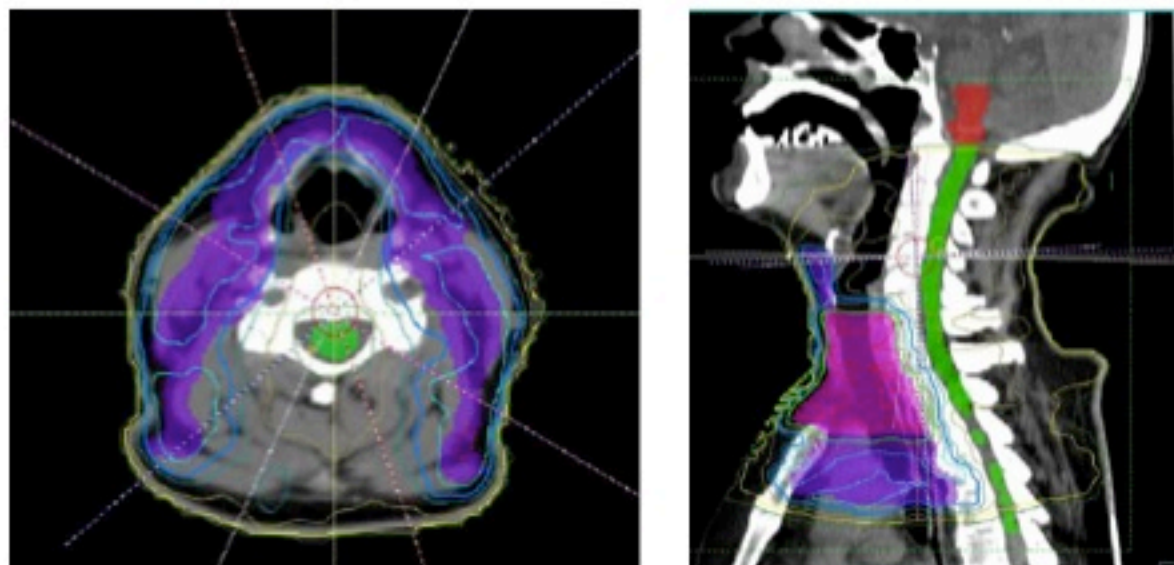


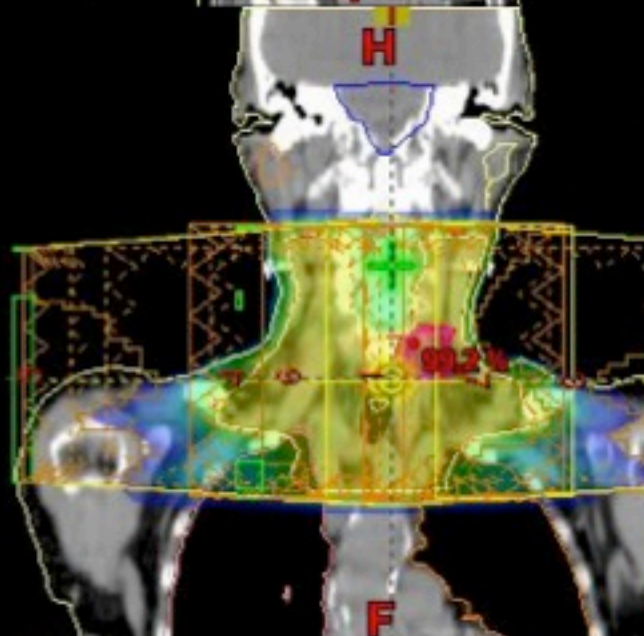
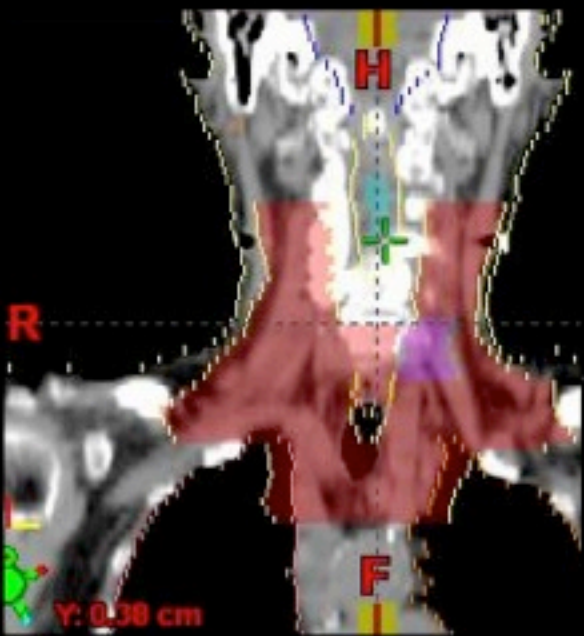
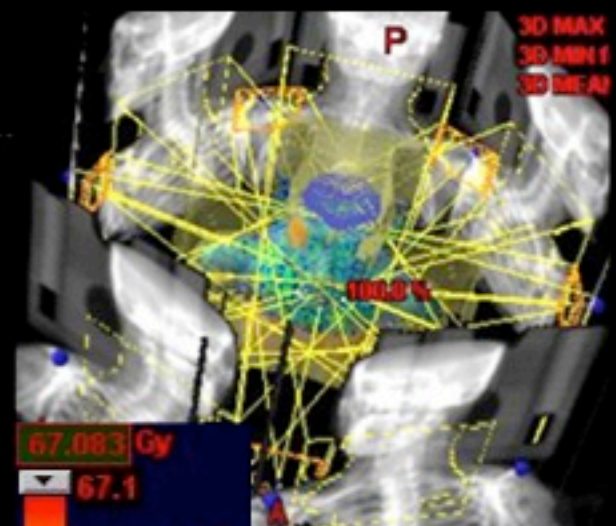
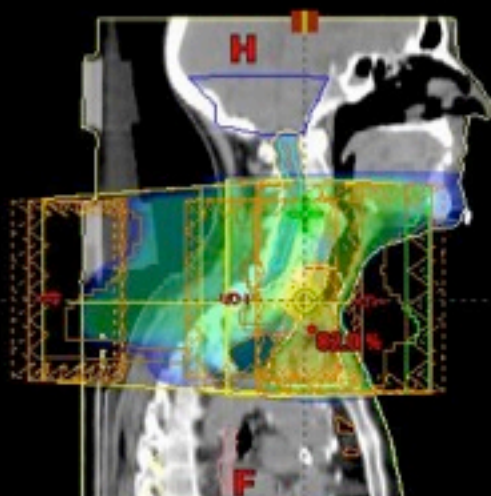
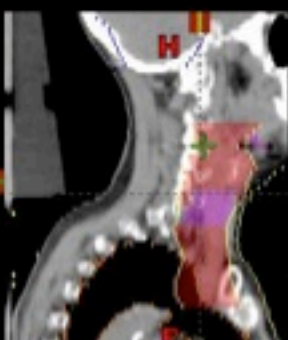
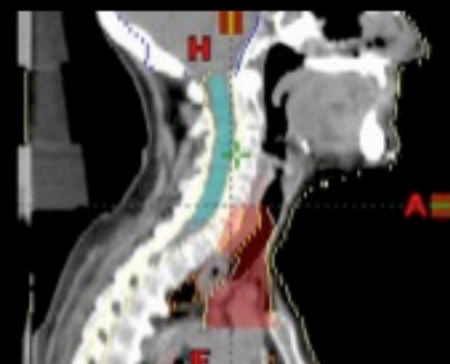
Fig. 1. Simultaneous-integrated-boost (SIB)-IMRT technique characterised by the delivery of a different dose per fraction to different target volumes. Primary target volume (PTV1: dark grey) and elective nodal target volume (PTV2: light grey). The light grey line represents the 95% isodose and the dark grey line the 90% isodose for the 58.8 Gy prescription. The dark blue line represents the 95% isodose and the dark green line the 90% isodose for the 50.0 Gy prescription.

Improvements in target coverage and reduced spinal cord irradiation using intensity-modulated radiotherapy (IMRT) in patients with carcinoma of the thyroid gland

Christopher M. Nutting^{a,*}, David J. Convery^c, Vivian P. Cosgrove^c, Carl Rowbottom^c, Louiza Vini^b, Clive Harmer^b, David P. Deamaley^a, Steve Webb^c

	Prescription	PTV mean	PTV min	PTV max	Dose range (%)	Spinal cord (maximum)
Conventional RT	60	57.6(±0.9)	41.2(±8.2)	63.6(±1.4)	32.6(±14.4)	46.0(±1.5)
3DCRT	60	57.2(±0.4)	46.3(±5.6)	63.6(±1.4)	29.1(±9.1)	46.0(±1.1)
Nine-field IMRT	60	59.8(±0.2)	55.2(±1.2)	64.6(±0.8)	15.7(±2.9)	40.7(±0.2)
		$P < 0.01$	$P = 0.02$	$P = 0.3$	$P < 0.01$	$P < 0.01$
Seven-field IMRT	60	59.8(±0.1)	55.3(±1.1)	64.6(±1.1)	15.5(±3.3)	40.4(±0.7)
Five-field IMRT	60	59.8(±0.1)	54.3(±1.7)	65.3(±1.2)	18.3(±4.6)	41.0(±1.0)
Three-field IMRT	60	59.6(±0.2)	52.2(±1.3)	66.0(±1.1)	23.0(±3.7)	42.6(±0.5)

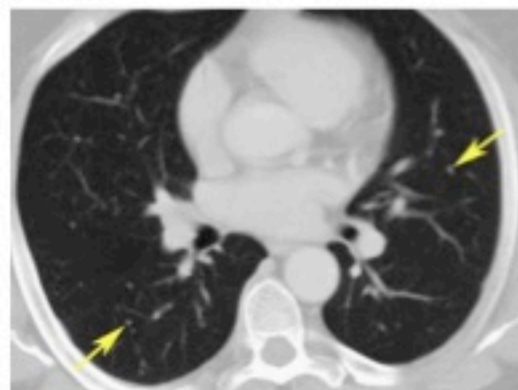
	Loco-regional lymph nodes mean dose (range)	Thyroid bed mean dose (range)	Total thyroid bed mean dose	Total spinal cord dose (maximum)
Conventional RT	39.6 (34.7–42.9)	12.5 (7.2–14.5)	52.1	46.0
3DCRT	39.3 (34.4–42.3)	12.5 (6.7–14.5)	51.8	46.0
Nine-field IMRT	45.7 (39.7–50.0)	14.0 (12.7–19.8)	59.7	42.1
Nine-field SIB	48.9 (42.8–60)	–	59.7	44.9
	$P < 0.01$	$P < 0.01$	$P < 0.01$	$P < 0.01$

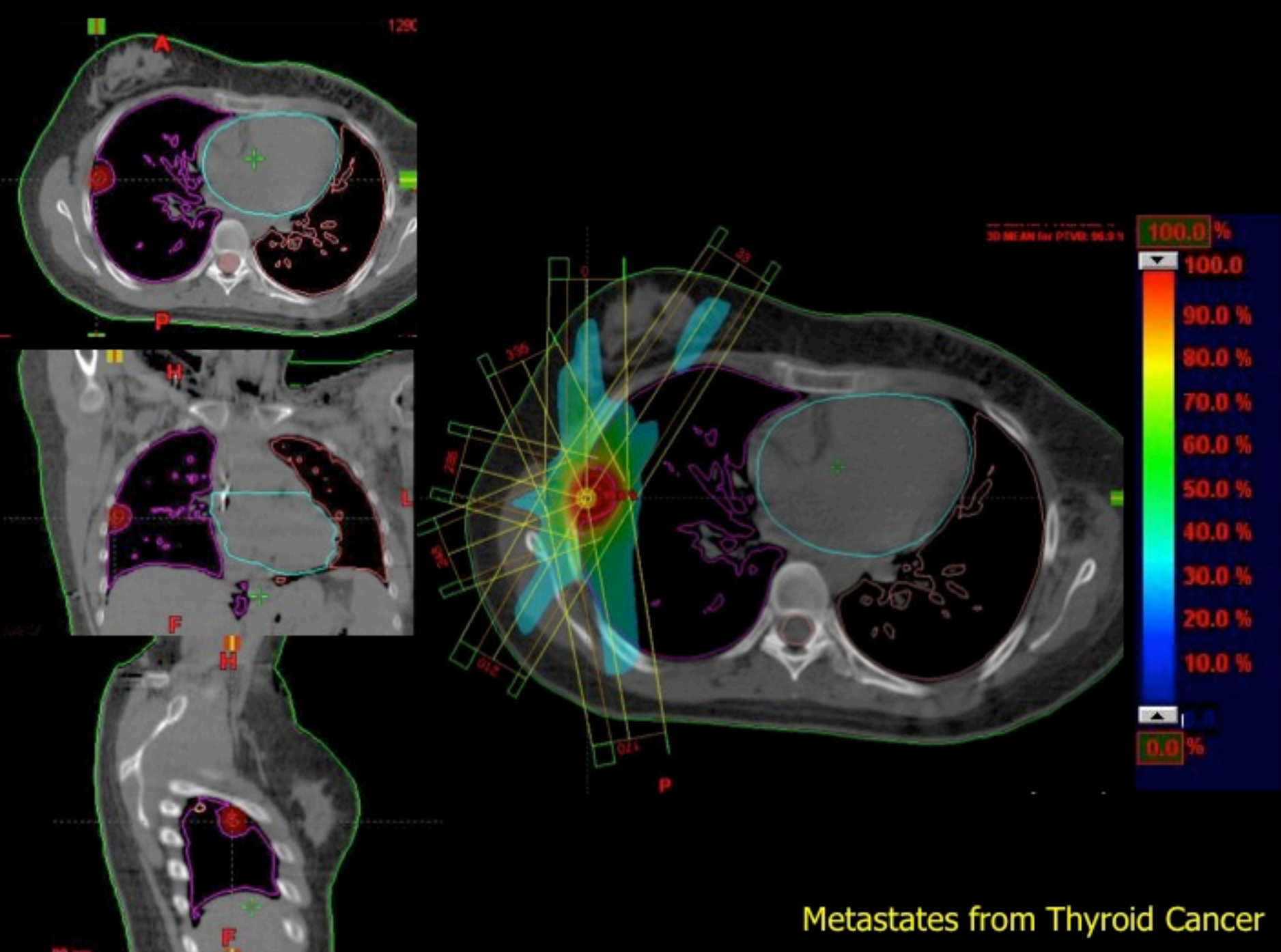


➤ *Carcinoma della tiroide differenziato*

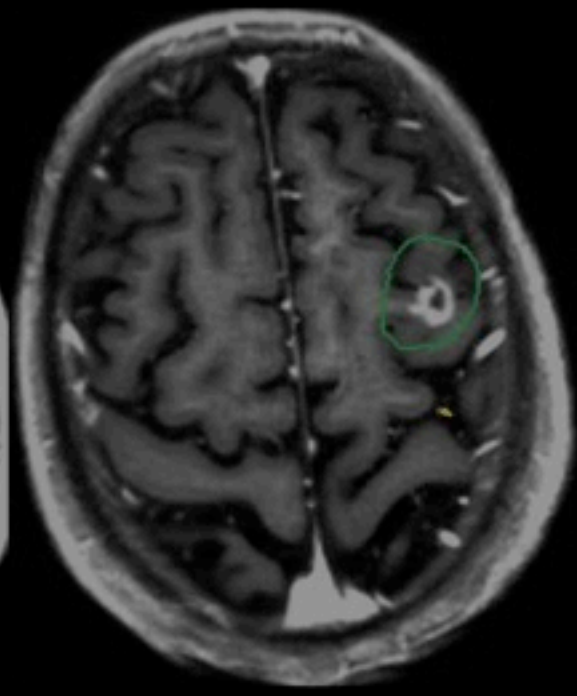
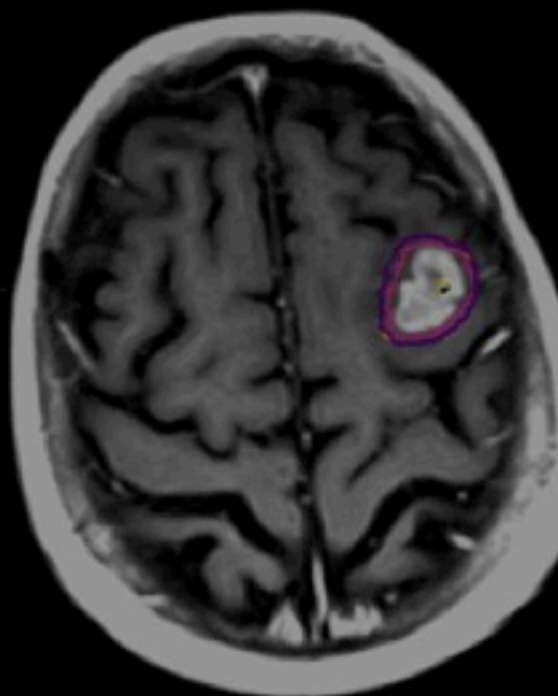
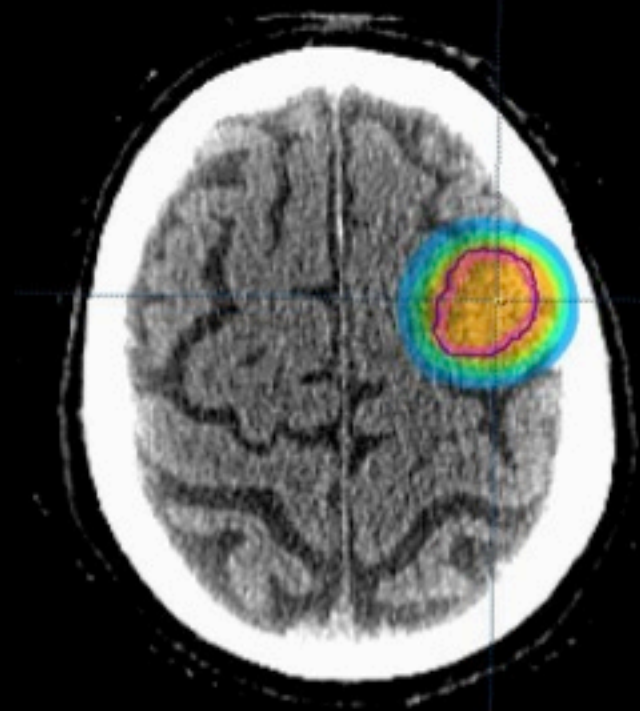
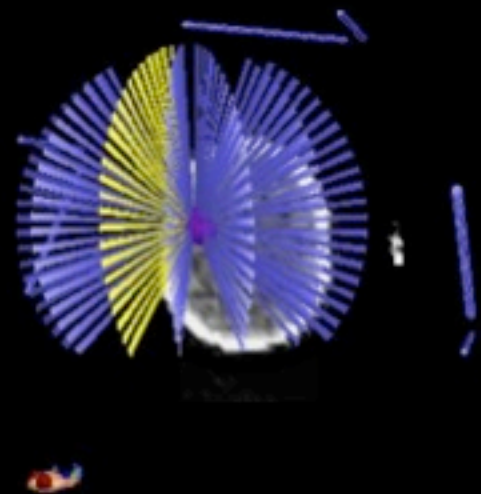
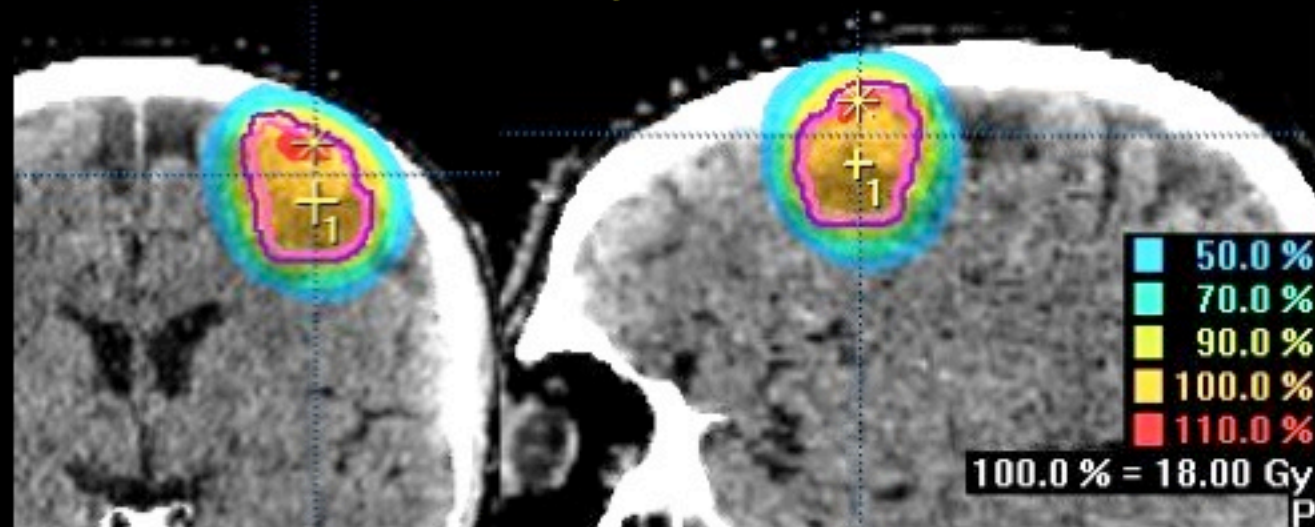
➤ *metastasi a distanza*

- ✓ *Rappresentano il 21% di tutte le recidive*
- ✓ *Il 50% di questi pz. muore a causa del tumore*
- ✓ *63% con unica localizzazione polmonare*



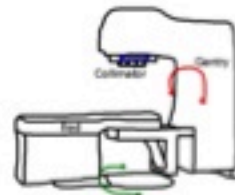


Brain metastastes from Thyroid Cancer



carcinoma differenziato della tiroide: summary

➤ Non iodocaptanti EBRT indicata:



- ✓ *Residui di malattia nel campo chirurgico*
- ✓ *Interessamento del tessuto connettivo*
- ✓ *Infiltrazione estesa dei linfonodi cervicali*

➤ Iodocaptanti pT4, N+, ≥45aa:

- ✓ *Nei pz di tutte le età con recidiva di malattia*
- ✓ *Metastasi ossee isolate dopo terapia con radioiodio*
- ✓ *Lesioni non iodocaptanti*
- ✓ *Metastasi cerebrali*

Carcinoma anaplastico della tiroide

- ✓ *Rapida e progressiva progressione locale con diffusione ai linfonodi regionali*
- ✓ *Prognosi infausta con una mediana di sopravvivenza di 6 mesi dalla comparsa dei sintomi*
- ✓ *Escissione chirurgica raramente praticabile*
- ✓ *E' il meno radiosensibile di tutti i tumori della tiroide*

- EBRT nel carcinoma anaplastico della tiroide*

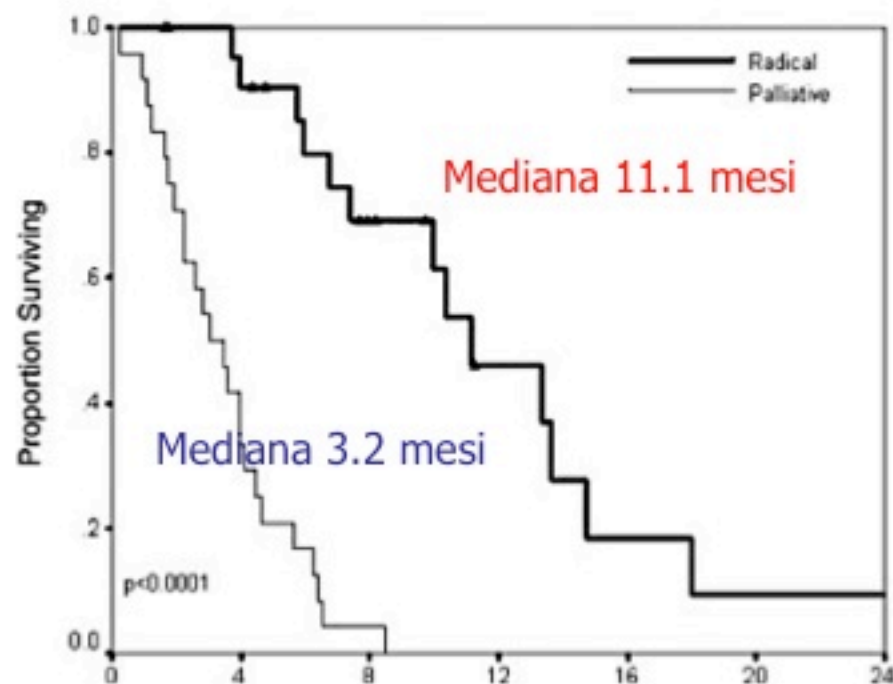
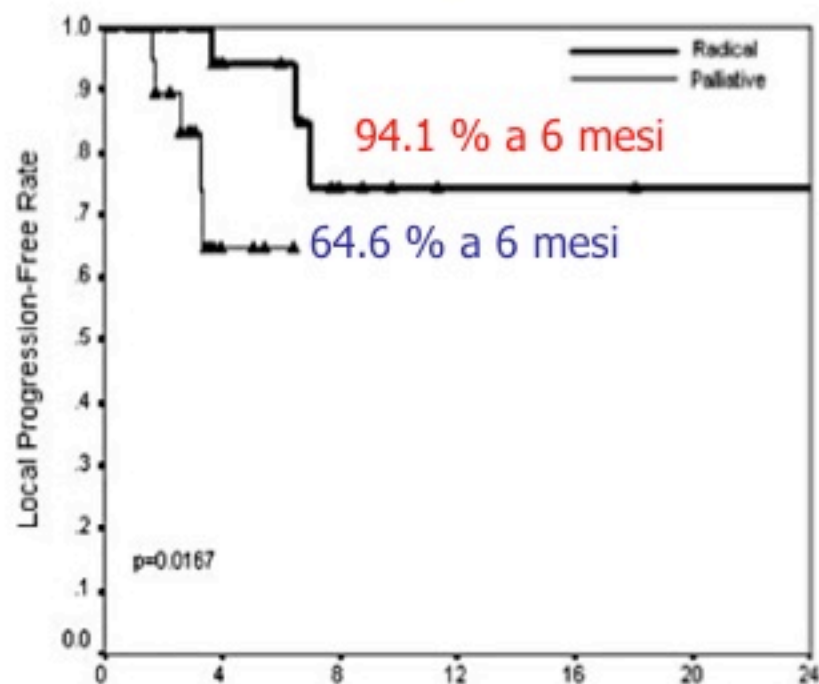
Published Series of Anaplastic Thyroid Carcinoma Studies That Have Categorized Treatment Modalities

Series	Year	No.	Treatment modalities					Overall survival (mos)	No. of survivors > 2 yrs (%)	No. of survivors > 2 yrs with curative resection (%)
			None	S only	C/R only	C/R → S	S → C/R			
Jereb et al. ¹	1975	79	5	7	38	0	27	2.5 ^a (mean)	1 (1)	1 (100)
Aldinger et al. ⁹	1978	84	17	16	19	0	28	6.2 (mean)	8 (10)	6 (75)
Simpson ²⁰	1980	94	7	1	40	0	46	NR	0	—
Kim and Leeper ²¹	1983	9	0	0	3	6	0	10 ^a (mean)	0	—
Spires et al. ²	1988	14	2	0	3	0	9	4 (median)	0	—
Demeter et al. ¹⁰	1991	17	0	3	0	0	14	12 (median)	5 (29)	4 (80)
Schlumberger et al. ¹¹	1991	20	0	0	8	1	11	NR	2 (10)	2 (100)
Junor et al. ³	1992	91	0	5	58	0	28	5 (median)	10 (11)	NR
Tan et al. ⁴	1995	21	2	1	9	0	9	4.5 (median)	3 (14)	3 (100)
Kobayashi et al. ¹²	1996	37	1	0	12	0	24	NR	3 (8)	3 (100)
Nilsson et al. ⁶	1998	81	0	0	32	48 ^b	1	4.3 ^a (mean)	8 (10)	NR
Lo et al. ⁵	1999	28	0	18	0	1	9	2.3 ^a (median)	1 (4)	NR

Clinical Outcome of Anaplastic Thyroid Carcinoma Treated With Radiotherapy of Once- and Twice-Daily Fractionation Regimens

2006 American Cancer Society

➤ *radical RT vs palliative RT*

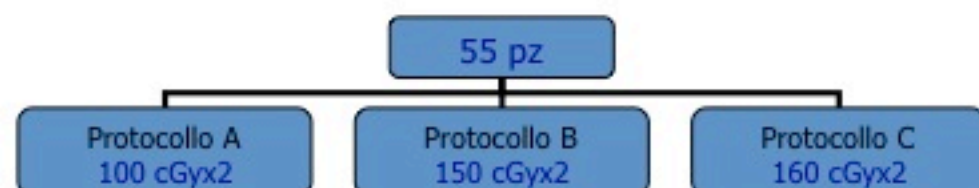


Carcinoma anaplastico

- *RT iperfrazionata, doxorubicina seguita da intervento di debulking (33 pz).*
- ✓ *Controllo locale 50%*
- ✓ *24% decessi dovuti a recidiva locale*
- ✓ *Sopravvivenza mediana 4.5 mesi*
- ✓ *solo 4 sopravvissuti >2 years*

Anaplastic thyroid carcinoma: three protocols combining doxorubicin, hyperfractionated radiotherapy and surgery

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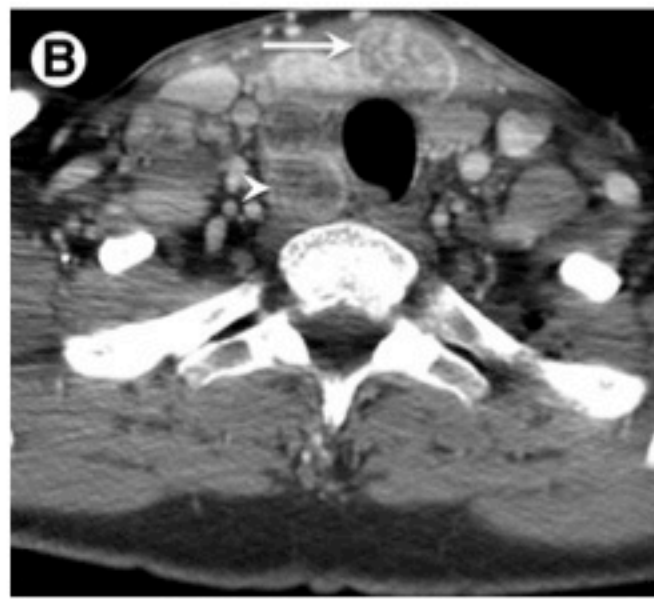
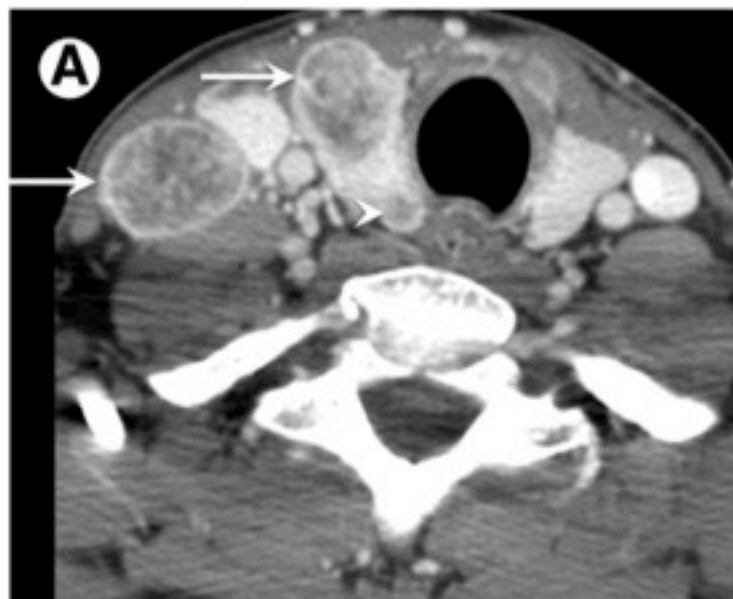


<i>Protocollo</i>	<i>A</i>	<i>B</i>	<i>C</i>
<i>Sopravvivenza media (mesi)</i>	3.5	4.5	2
<i>Controllo locale</i>	5/16	11/17	17/22

- ✓ *Miglior controllo locale nel gruppo C*
- ✓ *Correlazione positiva tra radioterapia accelerata e controllo locale*

Carcinoma midollare

- *L'uso della EBRT adiuvante è raccomandato*
- ✓ *Pz con malattia localmente avanzata*
- ✓ *Pz con interessamento linfonodale multiplo che mostrano una persistenza di elevati valori postoperatori della calcitonina indicanti la presenza di malattia microscopica residua*
- ✓ *Può essere presa in considerazione con tumori bulky inoperabili*
- ✓ *Recidiva postoperatoria*



CT of medullary carcinoma: T1N1b, 49-year-old man with palpable right thyroid mass.

(A) Axial contrast-enhanced computed tomography (CECT) shows a dominant 2.5-cm mass in the right thyroid lobe (top arrow). There is multifocal disease with a smaller nodule in the posterior right lobe near the tracheoesophageal groove (arrowhead). There is a heterogeneous level IV lymph node metastasis (bottom arrow).

(B) Lower axial CECT image shows a delphian node (arrow) and right paratracheal lymph nodes (arrowhead).

..Grazie per l'attenzione..



Questions