



Associazione
Italiana
Radioterapia
Oncologica

XXI CONGRESSO NAZIONALE AIRO

Genova, 19-22 novembre 2011

Porto Antico di Genova

Centro Congressi

SIMPOSIO AIRO-AIOM

ATTUALITA' NEL TRATTAMENTO DEI TUMORI TESTICOLARI

SEMINOMA I STADIO STANDARD TERAPEUTICI

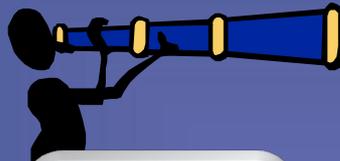
Silvia Tana

SC Radioterapia 2
Fondazione IRCCS
Istituto Tumori Milano

STRATEGIE POST CHIRURGICHE



...'50



'80



'90-'00



'00

SEMINOMA I STADIO

STRATEGIE POST CHIRURGICHE



trattamento standard per
diversi decenni e
termine di paragone per
le opzioni alternative



RAZIONALE

Radiosensibilità dell'istotipo
Diffusione lungo bersagli precisi
Rara diffusione a distanza

CARATTERISTICHE OTTIMALI
PER IL TRATTAMENTO RADIANTE



STATO DELL'ARTE

Tableau 6. Intérêt de la radiothérapie adjuvante. Results with adjuvant radiotherapy.

Étude	Nombre de patients	Suivi médian (mois)	Technique de radiothérapie	Rechutes (%)	Survie spécifique (%)
Bayens et al. [136]	132	88	Dogleg	4,5	99
Coleman et al. [71]	144	–	Dogleg	4,2	100
Fossa et al. [62]	478	54	Dogleg ou lombo-aortique	3,8	100
Jones et al. [63]	625	61	Dogleg ou lombo-aortique	3,4	99,9
Santoni et al. [72]	487	113	Dogleg ou lombo-aortique	4,3	99,4
Warde et al. [73]	283	122	Dogleg	4,9	99,7
Abdeen et al. [137]	52	75	Dogleg	3,8	96
Classen et al. [58]	675	61	Lombo-aortique	3,8	99,6
Oliver et al. [76]	904	78	Dogleg ou lombo-aortique	4	99,9



ricadute
eccezionali nel
volume irradiato

FU
più leggero

N mediastino,
SC, inguini.
M polmone



With a cause-specific survival rate of 100%,
the question has become not
'how can the disease be cured?'
but rather
'how can we retain this excellent cure rate
at the least risk of short- and long-term
consequences?'

TOSSICITA'



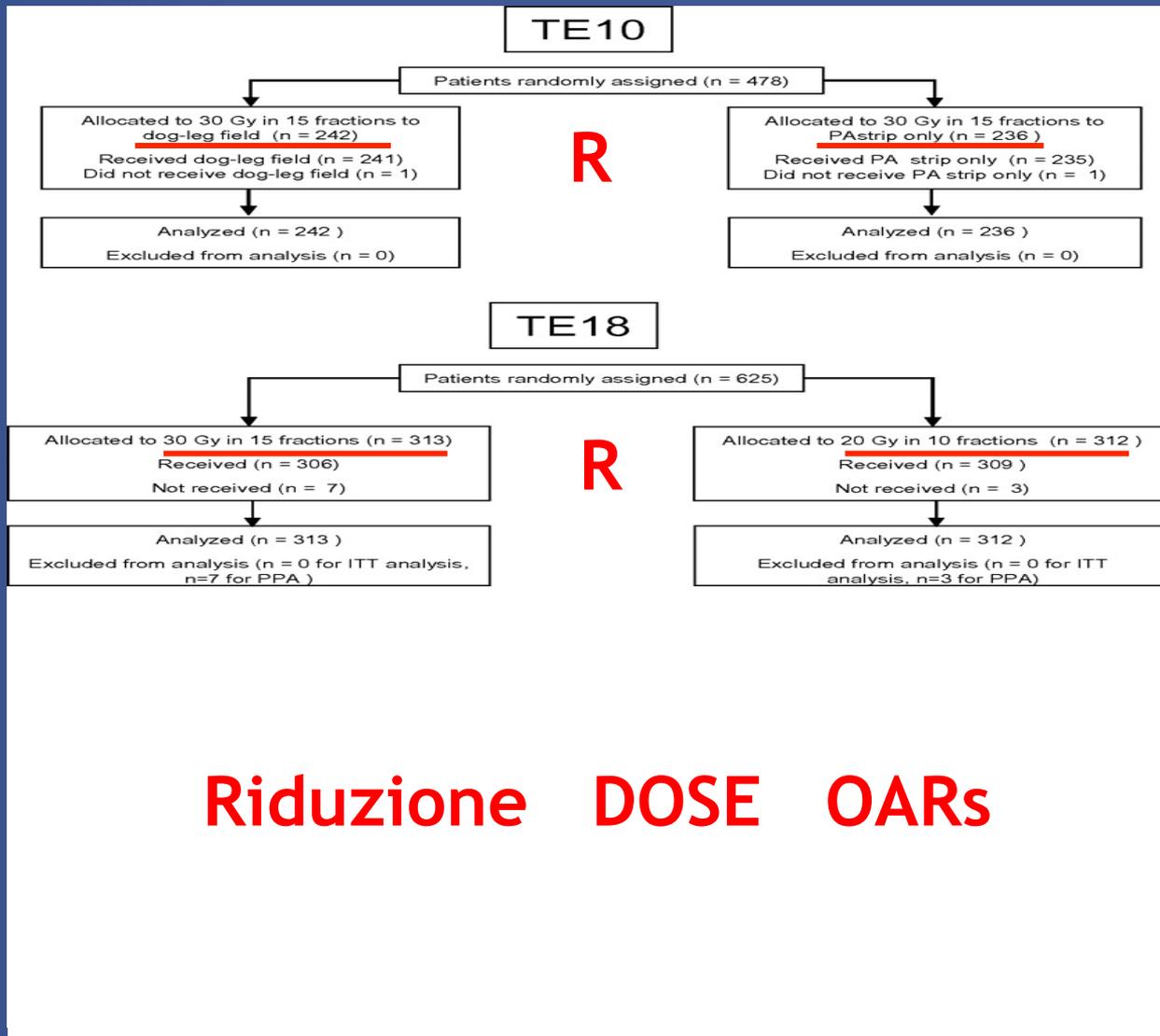
TOSSICITA'

neoplasie radioindotte

cardiovascolare

spermatogenesi

RT A VOLUME E DOSE RIDOTTI



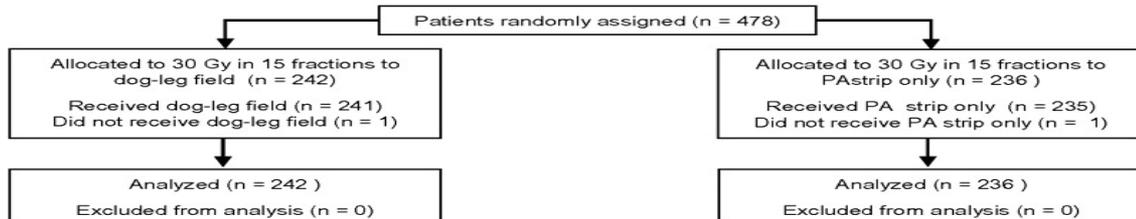
RAZIONALE
in assenza di malattia
PA, il coinvolgimento
degli N pelvici è
estremamente raro

RAZIONALE
istotipo radiosensibile
consente la riduzione
di dose

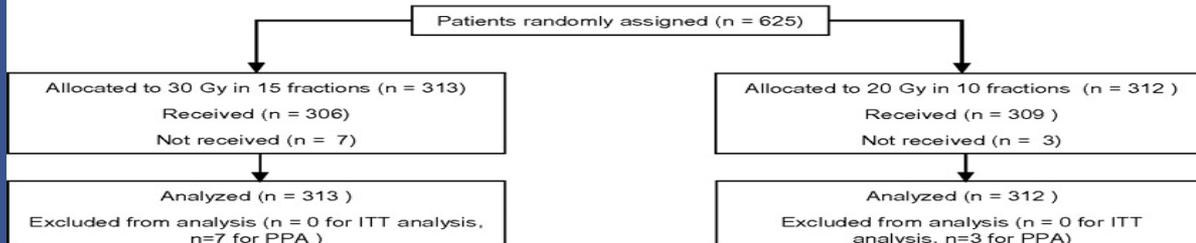
Riduzione DOSE OARs

RT A VOLUME E DOSE RIDOTTI

TE10



TE18



1 Fossa SD J Clin Oncol, 1999

2 Jones WG J Clin Oncol, 2005

1 RICADUTE

DL 9 (3,4%) 0 pelviche
PAS 9 (4%) 4 pelviche
a 7, 21, 23, 31 mos
tutti recuperati con CT/RT

2 30 Gy 20 Gy

10 ricadute 11
96,8% 2yRFS 97,5%
1,3% a favore 20 Gy

DOSE MEDIA ALLA GONADE

in funzione della lunghezza dei fasci

PAS

DL

0,09 Gy

$p < .001$

0,32 Gy

Dose totale alla gonade per un trattamento di 30 Gy/15 fr

Jacobsen KD Int J Radiat Oncol Biol Phys, 1997

0,0186 Gy

$p < .001$

0,0389 Gy

Dose alla gonade per singola frazione 180 cGy

Bieri S Radiother Oncol, 1999

DOSE E VOLUME RIDOTTI



Minore dose OARs
(pelvi, gonade)

Verosimile
riduzione neoplasie
radioindotte

**progresso
tecnologico**

Recupero più rapido
della fertilità
(13 vs 20 mos)

Fossa SD J Clin Oncol, 1999

Jones WG J Clin Oncol, 2005

Jacobsen KD Int J Radiat Biol Phys, 1997

Il recupero del danno e il ripristino della fertilità si completa generalmente in 12 - 24 mesi ed è condizionato dalla situazione pre -trattamento

La oligospermia pur transitoria può **impattare negativamente sulla QoL** nei pazienti con seminoma (età media di insorgenza 35 a)

VOLUME RIDOTTO CRITICITA'

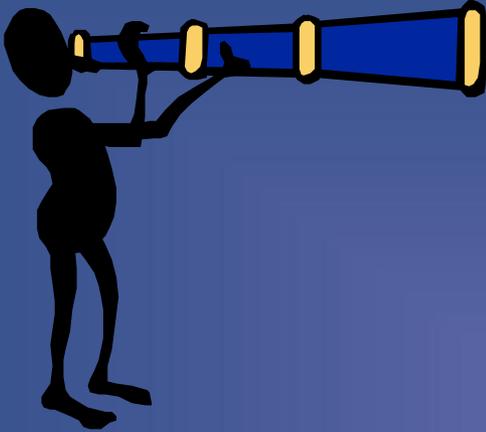


CT scan pelvi

per quanto
tempo ?

timing ?

Christie Hospital (339pz)
dimensioni medie dei linfonodi al momento
della diagnosi di ricaduta > 5 cm



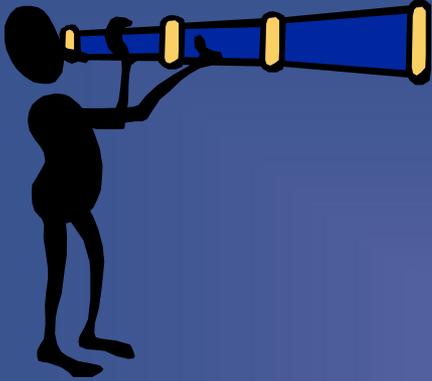
RAZIONALE

EVITARE TERAPIE ADIUVANTI

POTENZIALMENTE DANNOSE

RISERVANDO IL TRATTAMENTO SOLO

ALL'EVIDENZA DI MALATTIA



STATO DELL'ARTE

nessuno
random

Table 1
Outcomes for patients with stage I seminoma enrolled on surveillance programs

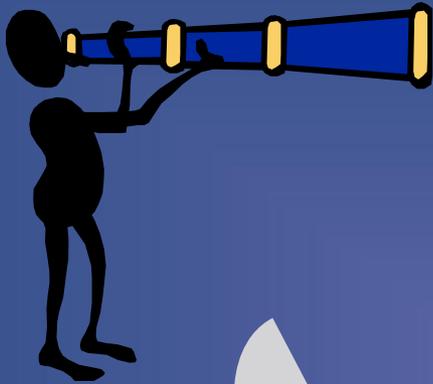
Author	Year	Median Follow-up (mo)	Number of Patients	Relapse (Number of Patients)	Relapse (%)	Cause-Specific Survival (%)
Horwich et al ¹⁰	1992	62	103	17	16.5	100.0
Ramakrishnan et al ¹¹	1992	44	72	13	18.0	100.0
Von der Maase et al ¹²	1993	48	261	49	18.8	98.9
Oliver et al ⁶	2001	98	110	21	19.0	100.0
Germa-Lluch et al ⁹	2002	33	233	38	16.0	100.0
Daugaard et al ⁸	2003	60	394	69	17.5	100.0
Warde et al ⁷	2005	98	421	64	15.2	99.7
Yoshida et al ¹⁴	2009	124	64	7	11.0	98.4
Kamba et al ¹³	2010	45	186	19	10.0	100.0

Fattori Predittivi di Recidiva

Seminoma (livello 4 C):

- Diametro di T (4 cm)
- Infiltrazione *Rete Testis*

Warde P et al. J Clin Oncol; 20:4448-4452 2002



FR -

**ricadute
6-12%**

Warde P J Clin Oncol, 2002

Aparicio J J Clin Oncol, 2005

RISK-ADAPTED MANAGEMENT CRITICITA'

However, prognostic criteria
have not yet been

validated in an independent data set

(in fact a recent study failed to validate them), and
there are doubts as to whether they provide
sufficient discrimination.

Chung PW J Clin Oncol, 2010

Consequently, risk stratification cannot be fully
endorsed at present.

Skiliarenko J Int J Urol, 2009

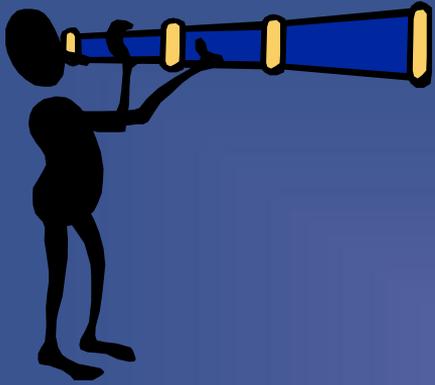


all'80-90% dei pazienti
si evita un trattamento
inutile e
potenzialmente dannoso

ricadute
principalmente
nel distretto PA

RT/CT

OS >99%



CRITICITA'

marcatori
ricadute tardive

FU
impegnativo
protratto

compliance

rischio diagnosi tardiva
o abbandono del FU
stress psicologico

RICADUTE TARDIVE

Dagli studi di sorveglianza sappiamo che
il 30 % delle ricadute avviene dopo il secondo anno
e il 5 % dopo il quinto anno



CRITICITA'

radioprotezione

Table 1

Average* effective doses of radiation for various diagnostic radiology procedures⁹⁻¹¹

Procedure†	Average effective dose of radiation (mSv)	Equivalent number of radiographs	Equivalent period of average natural background radiation (days)
Posteroanterior chest radiography	0.02	1	3
Skull radiography	0.1	5	15
Mammography	0.4	20	61
Pelvic radiography	0.6	30	91
Abdominal radiography	0.7	35	106
Lung perfusion scintigraphy (^{99m} Tc-MMA)	2.0	100	304
CT brain	2.0	100	304
Intravenous urography	3.0	150	456
Bone isotope scintigraphy (^{99m} Tc-MDP)	6.3	315	958
CT chest	7.0	350	1065
CT abdomen	8.0	400	1217
Barium enema	8.0	400	1217
CT pulmonary angiography	15.0	750	2281
CT coronary angiography	16.0	800	2433

BMJ. 2011 Feb 25;342:d947. doi: 10.1136/bmj.d947.

The risks of radiation exposure related to diagnostic imaging and how to minimise them.

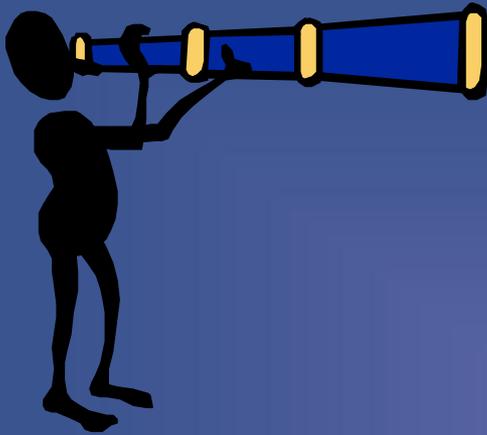
Davies HE, Wathen CG, Gleeson FV.

Department of Respiratory Medicine, University Hospital of Wales, Vale of Glamorgan CF64 2XX, UK. hedavies@doctors.net.uk

Table 2

Typical organ specific radiation doses for various radiology procedures^{2,4}

Procedure	Organ	Organ specific radiation dose (mSv)
Posteroanterior chest radiography	Lung	0.01
Mammography	Breast	3.5
CT chest	Breast	21.4
CT coronary angiography	Breast	51.0
Abdominal radiography	Stomach	0.25
CT abdomen	Stomach	10.0
	Colon	4.0
Barium enema	Colon	15.0



CT scan/anno

EGCCCG 15/10 anni

NCCN 21/10 anni

ESMO 7/5 anni

EAU 7/5 anni

PMH 20/10 anni

RMH 20/10 anni

Austria 8-9/6 anni

Germania 4/2 anni

fino a 420 mSv

Association of Diagnostic Radiation Exposure and Second Abdominal-Pelvic Malignancies After Testicular Cancer

Carl van Walraven, Dean Fergusson, Craig Earle, Nancy Baxter, Shabbir Alibhai, Blair MacDonald, Alan J. Forster, and Ilias Cagiannos

Diagnosed with testicular cancer between
July 1, 1991 and December 31, 2004
(N = 3,819)

Diagnosis not from pathology
or cancer center registration
(n = 158; 4.1%)

Previous or
concomitant cancer
(n = 102; 2.7%)

Had retroperitoneal
lymph node dissection
(n = 51; 1.3%)

Had radiotherapy
(n = 255; 6.7%)

Did not have an
orchidectomy
(n = 296; 7.8%)

Age < 18 years
(n = 74; 1.9%)

Died within 5 years of diagnosis
(n = 115; 3.0%)

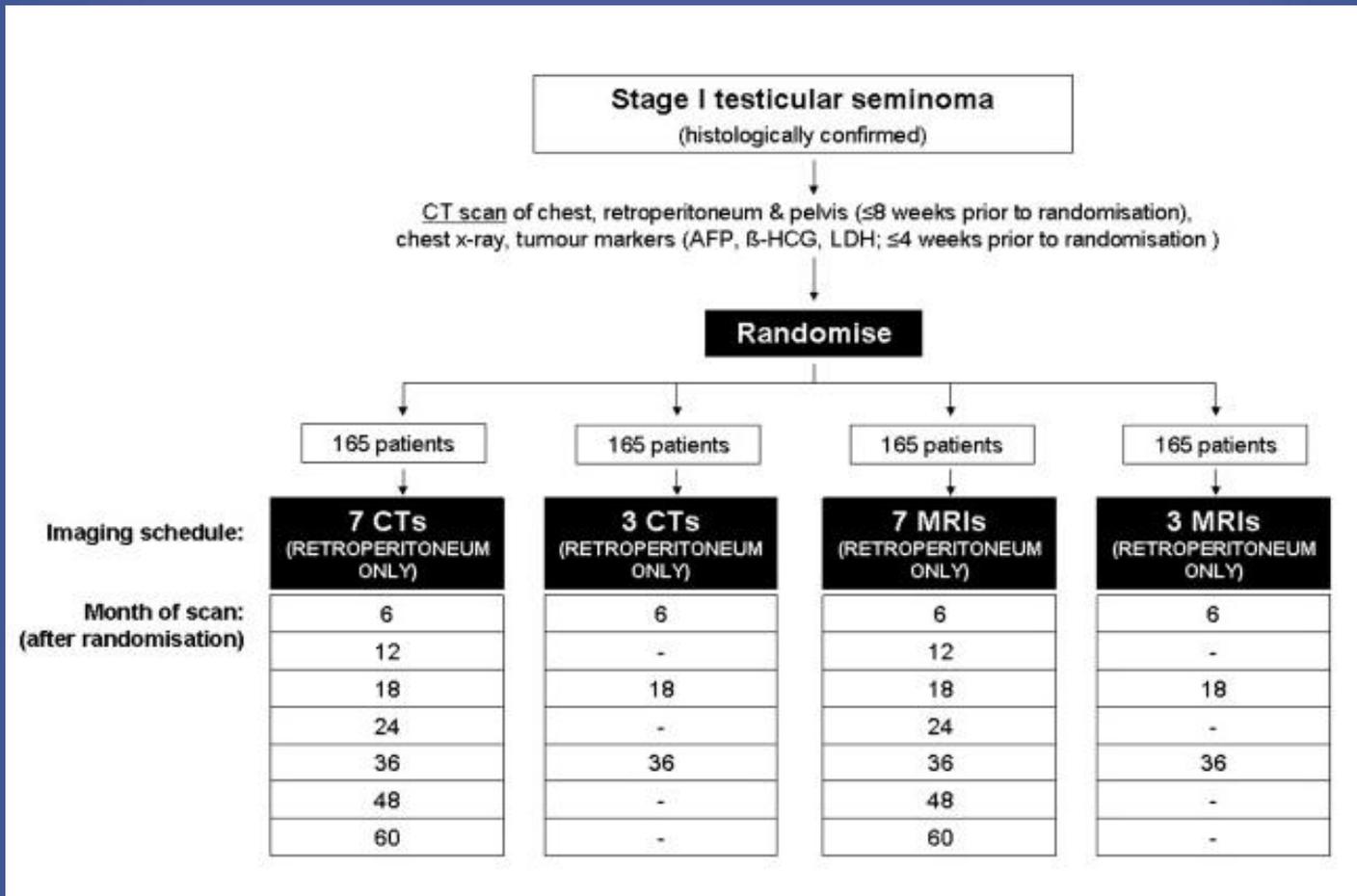
Developed 2nd malignancy within
5 years of diagnosis
(n = 199; 5.2%)

Included in analysis
(n = 2,569)

Results A total of 2,569 men (mean age, 34.7 years; standard deviation, 10.2) were observed for a median of 11.2 years (interquartile range [IQR], 8.3 to 14.3). During the first 5 years after diagnosis, men underwent a median of 10 computed tomography (CT) scans (IQR, 4 to 18) of the abdominal-pelvic area, and they were exposed to a median of 110 mSv of radiation from radiologic investigations (IQR, 44 to 190). After this, 14 men were diagnosed with a second abdominal-pelvic malignancy (rate, five per 10,000 patient-years observation, 95% CI, three to eight); the most common diagnoses were colorectal and kidney malignancies. Radiation exposure was not associated with an excess risk of second cancers (hazard ratio per 10 mSv increase, 0.99; 95% CI, 0.95 to 1.04). This association did not change if men observed for fewer than 5 years were included in the analysis (hazard ratio, 1.00; 95% CI, 0.96 to 1.04).

Conclusion Second malignancies of the abdomen-pelvis are uncommon in men with low-grade testicular cancer. In this study, the risk of second cancer was not associated with the amount of diagnostic radiation exposure.

TRISST MRC TE24





RAZIONALE

Istotipo chemiosensibile in
considerazione dell'elevato tasso
di risposta che si osserva
negli stadi avanzati (CDDP)



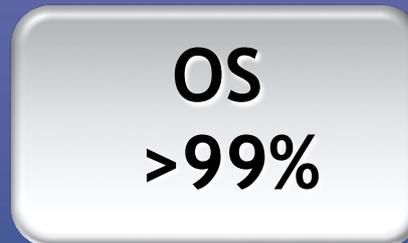
CARBOPLATINO

Table 3. Results of treatment with carboplatin in stage I seminoma.

Investigators	N	Courses of Carboplatin	Doses	Relapse n (%)	Follow-up, median months
Dieckmann et al. [47]	93	1	400 mg/m ²	8 (8.6)	48
Reiter et al. [48]	107	2	400 mg/m ²	0 (0)	74
Steiner et al. [49]	109	2	400 mg/m ²	2 (1.8)	60
Aparicio et al. [50]	60	2	400 mg/m ⁴	2 (3.3)	52
Oliver et al. [51]	560	1	7 AUC	27 (4.8)	48
Krege et al. [52]	43	2	400 mg/m ²	0 (0)	28
Aparicio et al. [58]	214	2	7 AUC	7 (3.3)	34

Total dose (mg) = [target AUC] × [glomerular filtration rate + 25] mg.

STRATEGIE POST CHIRURGICHE



Multidisciplinarietà
delle competenze

Linee Guida

ELEMENTI DI DECISIONE

Trattamenti
disponibili
Sorveglianza
RT
CT

Fattori di
rischio:
di recidiva
di tossicità
tardiva

Caratteristiche del
paziente:

Chi è
Cosa si aspetta

Partecipazione
del paziente
al processo
decisionale

Orientamenti di scuola
Expertise



Editorial

UK Management Practices in Stage I Seminoma and the Medical Research Council Trial of Imaging and Schedule in Seminoma Testis Managed with Surveillance

F.H. Cafferty^{*}, R. Gabe^{*}, R.A. Huddart[†], G. Rustin[‡], M.P. Williams[§], S.P. Stenning^{*},
A. Bara^{*}, R. Bathia^{*}, S.C. Freeman^{*}, L. Alder^{||}, J.K. Joffe[¶]

^{*} MRC Clinical Trials Unit, London, UK

[†] Institute of Cancer Research and the Royal Marsden Hospital, Sutton, UK

[‡] Mount Vernon Cancer Centre, Mount Vernon Hospital, Northwood, UK

[§] Derriford Hospital, Plymouth, UK

^{||} Nottingham University Hospitals, Nottingham, UK

[¶] St James' University Hospital, Leeds, UK

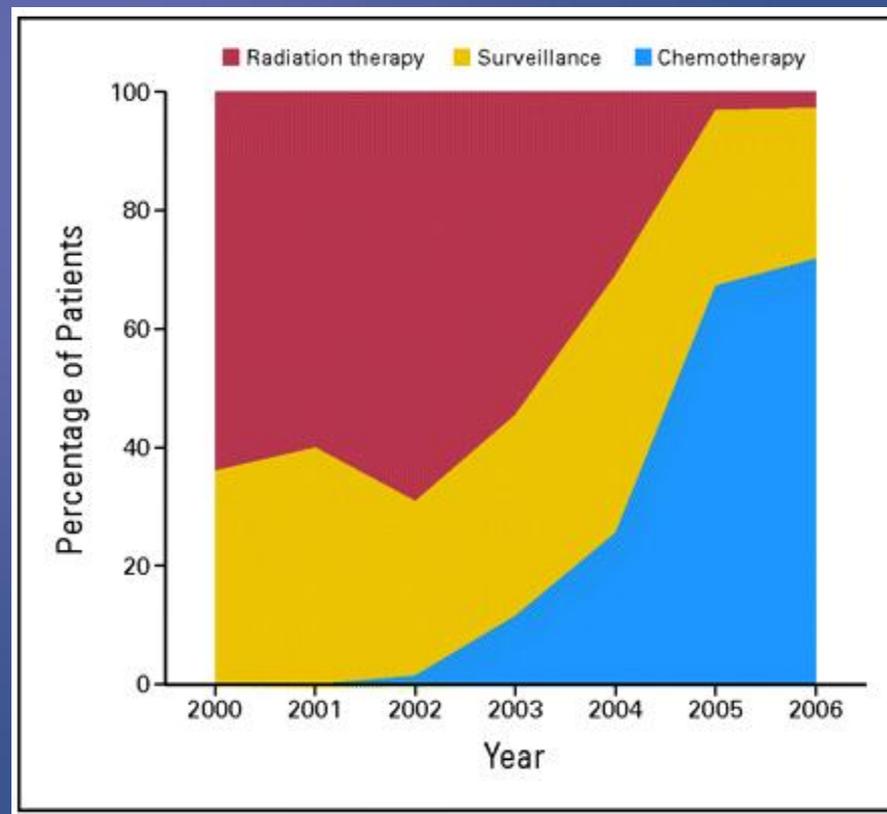
....Our surveys indicate that this decrease continued with only 8% of patients receiving radiotherapy in 2009 compared with 31% in 2005.

Similar declines have been reported worldwide.

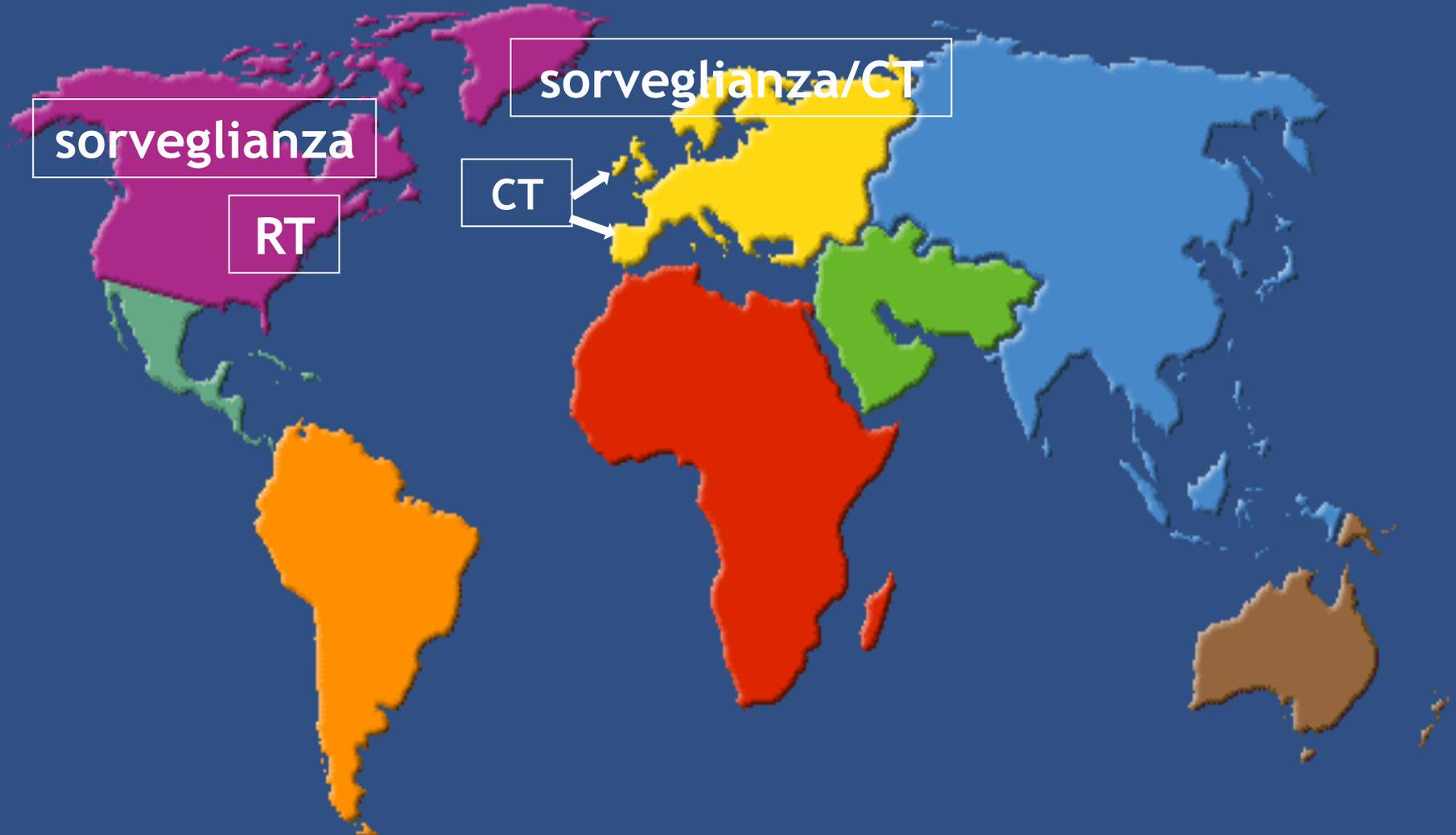
Management of Seminomatous Testicular Cancer: A Binational Prospective Population-Based Study From the Swedish Norwegian Testicular Cancer Study Group

Torgrim Tandstad, Rune Smaaland, Arne Solberg, Roy M. Bremnes, Carl W. Langberg, Anna Laurell, Ulrika K. Stierner, Olof Ståhl, Eva K. Cavallin-Ståhl, Olbjørn H. Klepp, Olav Dahl, and Gabriella Cohn-Cedermark

- Period: 2000-2006
- Policy: Surveillance/RT/CBCDA
- # pts: 1384
- Median FU: 62 mos
- Relapse: Surveillance 14.3
CBCDA 3.9%
RT 0.8%
- DSS: 99.6%



OPZIONI POST-CHIRURGICHE TREND





Seminoma I stadio

Quale è abitualmente la scelta terapeutica dopo chirurgia ?

survey 2006

67/143 46,8% di risposte

survey 2011

52/162 32% di risposte

sorveglianza in tutti i casi

0

Sorveglianza mirata

20 29,9%

RT in tutti i casi

47 70,1%

CT in tutti i casi

0

sorveglianza in tutti i casi

3 5,7%

Sorveglianza mirata

14 26,9%

RT in tutti i casi

32 61,5%

CT in tutti i casi

3 5,7%

Quale dose si prescrive abitualmente ?



survey 2006

survey 2011

20 Gy	10	14,9%
25-27 Gy	48	71,6%
30 Gy	9	13,4%

20 Gy	23	44,2%
25-27 Gy	29	55,8 %
30 Gy	0	



survey 2006

survey 2011

Quale volume viene abitualmente irradiato?

volume ridotto	40	61,5%
volume esteso	25	38,4%

Si estende l'irradiazione alle stazioni linfatiche inguinali/iliache controlaterali/scroto in caso di pregressi interventi chirurgici in regione inguino scrotale?

SI	31	46,9%
NO	35	53%

Quale volume viene abitualmente irradiato?

volume ridotto	38	73,1%
volume esteso	14	26,9%

Si estende l'irradiazione alle stazioni linfatiche inguinali/iliache controlaterali/scroto in caso di pregressi interventi chirurgici in regione inguino scrotale?

SI	30	57,6%
NO	22	42,4%

ISCRIZIONI

segretario@tumorigerminali.it



Italian
Germ cell cancer
Group



**GRAZIE PER
L'ATTENZIONE**