ROLE OF RADIATION IN SEMINOMATOUS TESTICULAR TUMORS

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INTRODUCTION:

- Testicular cancer is the most common malignancy in young men.
- Variation in incidence worldwide [In India 1% of all malignancy in males].
- >95% of germ cell tumors.
- 50% are seminoma.
- 90% stage I-IIB.
- Cure rates in stage I -100% .

PRE-TREATMENT EVALUATION

- Complete clinical examination (contralateral testis, s/c, abdomen, breasts)
- Routine tests include:

  1) Tumor markers: AFP, β-HCG, LDH, Baseline LH, FSH and testosterone.

  2) Chest X-ray, Ct-scan of Thorax, Abdomen and pelvis with i.v contrast/ MRI .
  3) FDG-PET : Useful in assessing significance of residual disease on CT after treatment (chemotherapy).

- Patients should be counselled for sperm banking.

HISTOLOGICAL CLASSIFICATION (WHO)

CN- Intratubular Germ Cell Neoplasia:

- Precursor lesion of most type of GCT (CIS / TIN).
- Abnormal germ cells within seminal tubules, found adjacent to testicular germ cell tu in >95% of cases.
- 50% risk of developing into invasive germ cell tumor within 5years.

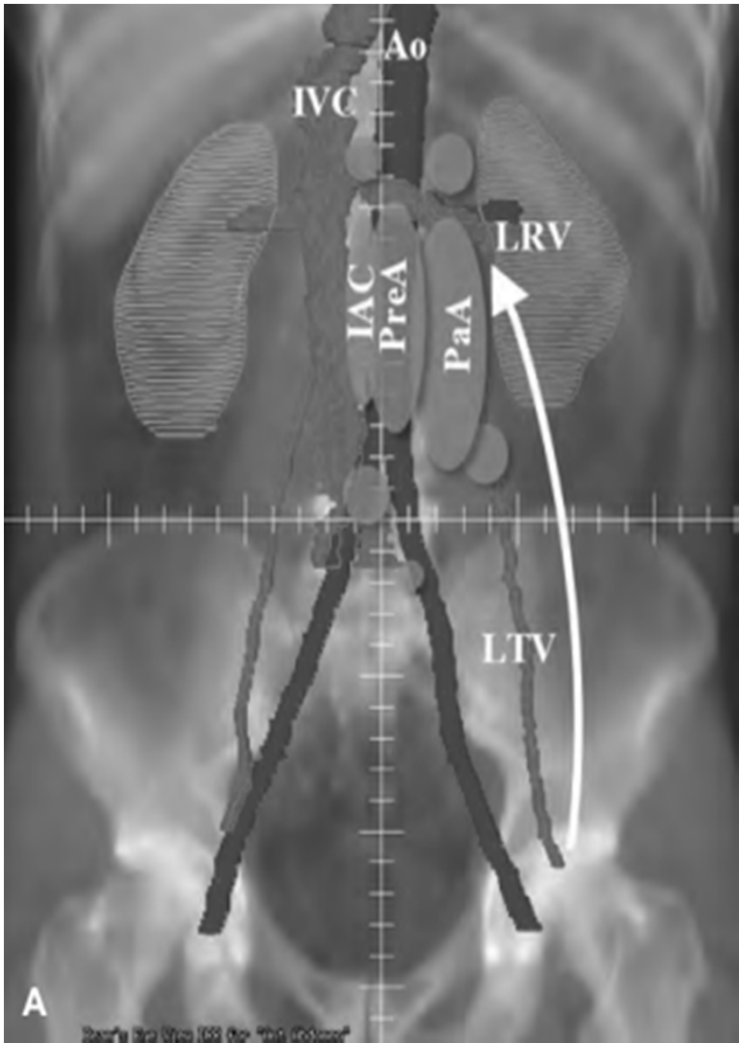
minoma-Classical type:

- Most common GCT (50%).
- β-HCG is elevated in 15-30%.
- AFP not elevated.

minoma- Spermatocytic type:

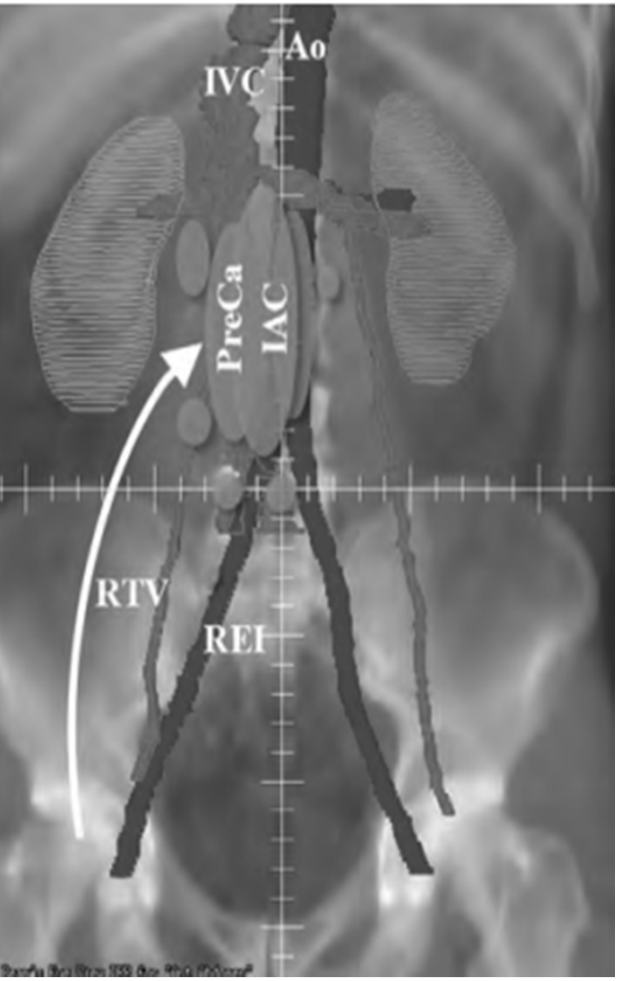
- 2 % of testicular tumor.
- Occurs at old age.
- Natural history and treatment- differs
- Confined to testis- orchiectomy.

LYMPHATIC DRAINAGE



- Left sided tumor:

from testis follows testicular arteries to para-aortic
renal hilar, retrocaval lymph nodes with contrala
node involvement 15-20%.



- Right sided tumor:

  follows inter-aortocaval, pre- caval & pre-aortic lymphnod

- From scrotum lymphatics drain into inguinal lymph nodes (may be disturbed by hernia repair, orchidopexy, scrotal surgery, pelvic infection).

- From retroperitoneal nodes cisterna chyli / thoracic duct left sub clavicular vein left supraclavicular node.

- **International Germ Cell Consensus Classification(IGCCC) for seminoma**

- In 1997, IGCCC defined staging system, based on independent clinical prognostic factors and categorised patients into

- Good Risk(90%):
  - 1) Normal AFP, Any β-HCG, Any LD
  - 2) Any Primary site
  - 3) No non-pulmonary, visceral metastasis present

- Intermediate Risk(10%):
  - 1) Non-pulmonary visceral metastasis present
  - 2) Any primary site
  - 3) Normal AFP, Any β-HCG, Any LDH

STAGING

Stage	Group
0	pTis, N0, M0, S0
IA	pT1, N0, M0, S0
IB	pT2–4, N0, M0, S0
IS	Any pT/Tx, N0, M0, S1–3
IIA	Any pT/Tx, N1, M0, S0–1
IIB	Any pT/Tx, N2, M0, S0–1
IIC	Any pT/Tx, N3, M0, S0–1
IIIA	Any pT/Tx, any N, M1a, S0–1
IIIA	Any pT/Tx, N1–3, M0, S2 Any pT/Tx, any N, M1a, S2
IIIC	Any pT/Tx, N1–3, M0, S3 Any pT/Tx, any N, M1a, S3 Any pT/Tx, any N, M1b, any S

RADIOTHERAPY IN TESTICULAR SEMINOMA

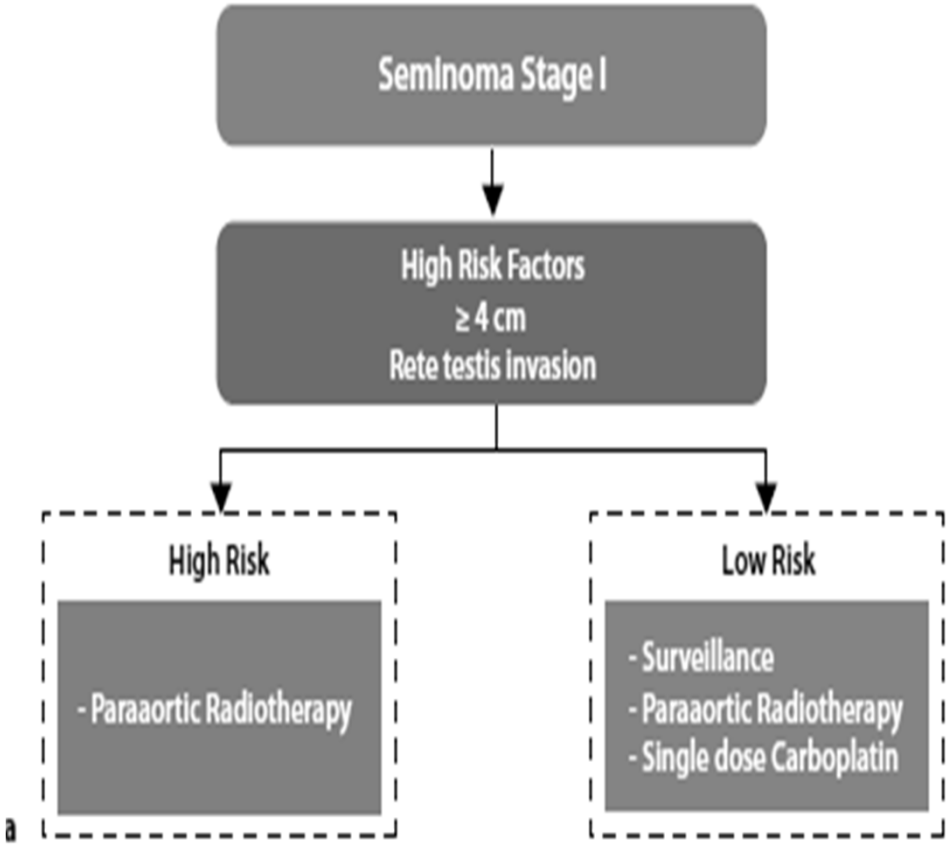
- The rationale for adjuvant radiotherapy is the high radiosensitivity of seminoma and the stepwise dissemination of tumor cells (via lymphatisystem in the retroperitoneum).

- This highly predictive tumor spread provides the basis for target volume definition of radiotherapy on the basis of anatomic land marks.

INDICATIONS – RADIOTHERAPY

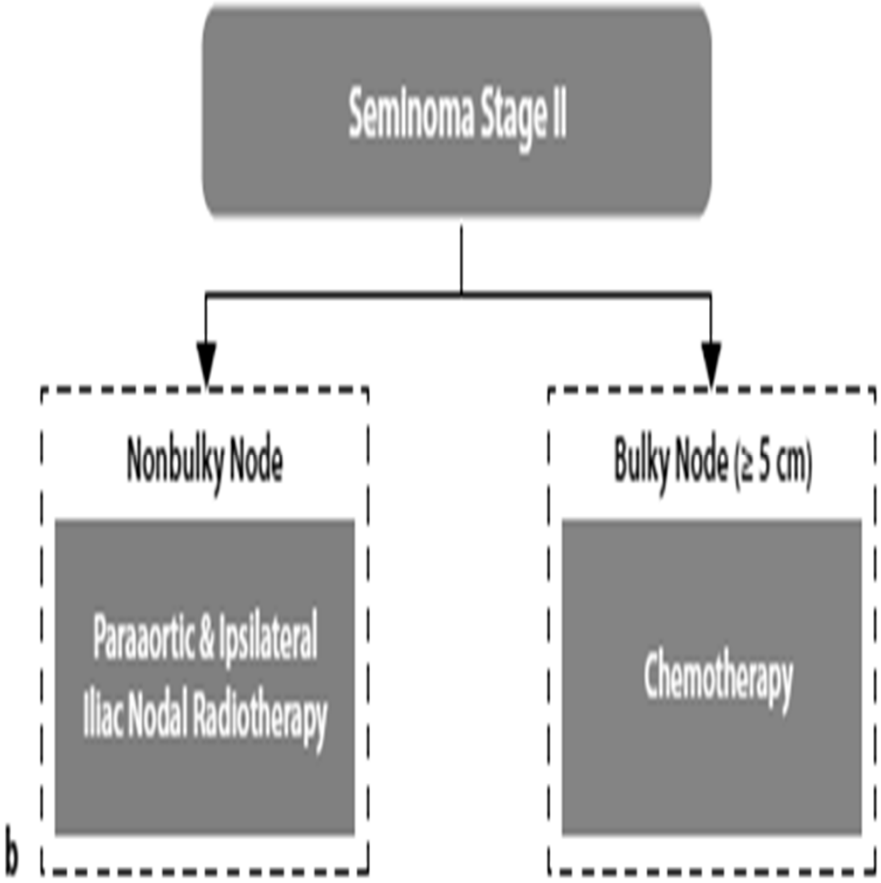
- Adjuvant therapy after orchiectomy for stages I–IIb diseases
- Salvage of locoregional failure after surgery or chemotherapy
- Palliative treatment to locoregional or distant metastatic sites

ADJUVANT RADIOTHERAPY STAGE I



- In clinical stage I seminoma, tumor size ≥4 cm is associated with approximately 30% risk of recurrence with surveillance alone.
- The current recommendation is EBRT- 20Gy/10# to the para-aortic strip.

ADJUVANT RADIOTHERAPY
STAGE II



- For patients with stage II seminoma, the recommended treatment depends on the bulk of retroperitoneal nodal disease.

- Radiotherapy to 25 to 35 Gy is the treatment of choice for patients with stage IIA or IIB seminoma (nodal disease ≤5 cm in maximal diameter).

- Irradiation of the para-aortic and ipsilateral pelvic nodes is a highly effective treatment strategy with a recurrence rate <10% and a disease-specific survival rate of 97% to 100%.

- Patients with stage IIC retroperitoneal disease (nodes >5 cm) are usually managed with systemic chemotherapy.

- Radiotherapy remains a treatment option, if the mass is centrally located and does not overlie most of one kidney or significantly overlap the liver.

- For nodal disease >10 cm in diameter, the relapse rate is >40% with radiotherapy and such patients should be managed with systemic chemotherapy.

Prognostic Factors for Relapse in Stage I Seminoma Managed by Surveillance: A Pooled Analysis

By Padraig Warde, Lena Specht, Alan Horwich, Tim Oliver, Tony Panzarella, Mary Gospodarowicz, and Hans von der Maase

- 638 patients from various center (Princess Margaret Hospital, Royal Marsden Hospital, and Royal London Hospital) were analysed for tumor characteristics (size, histologic subtype, invasion of rete testis, and tumor invasion into small vessels [SVI]) as well as age at diagnosis as a prognostic factor for relapse.
- With a median follow-up of 7.0 years, 121 relapses were observed.
- 5-year relapse-free rate (RFR) - 82.3%.
- On analysis-
- Tumor size (RFR: < 4 cm, 87%; > 4 cm, 76%; P .003).
- Rete testis invasion (RFR: 86% [absent] v 77% [present], P .003)
- The study concluded with identifying size of primary tumor and rete testis invasion as important prognostic factors for relapse in patients with stage I seminoma managed with surveillance.

VOLUME 29 · NUMBER 8 · MARCH 10 2011
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Trial of Carboplatin Versus Radiotherapy for Stage I Seminoma: Mature Results on Relapse and Contralateral Testis Cancer Rates in MRC TE19/EORTC 30982 Study (ISRCTN27163214)

R. Timothy D. Oliver, Graham M. Mead, Gordon J.S. Rustin, Johnathan K. Joffe, Nina Aass, Robert Coleman, Rhian Gabe, Philip Pollock, and Sally P. Stenning

- Randomized trial comparing carboplatin with radiotherapy (RT) as adjuvant treatment for stage I seminoma.
- Overall, 1,447 patients were randomly assigned (carboplatin, n = 573; RT, n = 904).
- RFRs at 5 years were 94.7% for carboplatin and 96.0% for RT.
- There was a clear reduction in the rate of contralateral GCTs – carboplatin

  n = 2, RT n = 15.

  The study concluded that results confirm the noninferiority of single dose carboplatin (at 7 × AUC dose) versus RT in terms of RFR and establish a statistically significant reduction in the medium term of risk of second GCT produced by this treatment.

DETERMINATION OF DOSE

VOLUME 23 · NUMBER 6 · FEBRUARY 20 2005
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Trial of 30 Versus 20 Gy in the Adjuvant Treatment of Stage I Testicular Seminoma: A Report on Medical Research Council Trial TE18, European Organisation for the Research and Treatment of Cancer Trial 30942 (ISRCTN18525328)

William G. Jones, Sophie D. Fossa, Graham M. Mead, J. Trevor Roberts, Michael Sokal, Alan Horwich, and Sally P. Stenning

- From 1995 to 1998, 625 patients were randomly assigned 20 Gy/10 fractions over 2 weeks or 30 Gy/15 fractions during 3 weeks after orchidectomy.
- Median follow-up of 61 months, 10 and 11 relapses, respectively, was reported in the 30- and 20-Gy groups.

- 5 year relapse free survival 97.0% after 30Gy
  96.4% after 20Gy

- The study concluded that treatment with 20 Gy in 10 fractions is unlikely to produce relapse rates more than 3% higher than for standard 30 Gy radiation therapy.

DETERMINATION OF TARGET VOLUME

Optimal Planning Target Volume for Stage I Testicular Seminoma: A Medical Research Council Randomized Trial

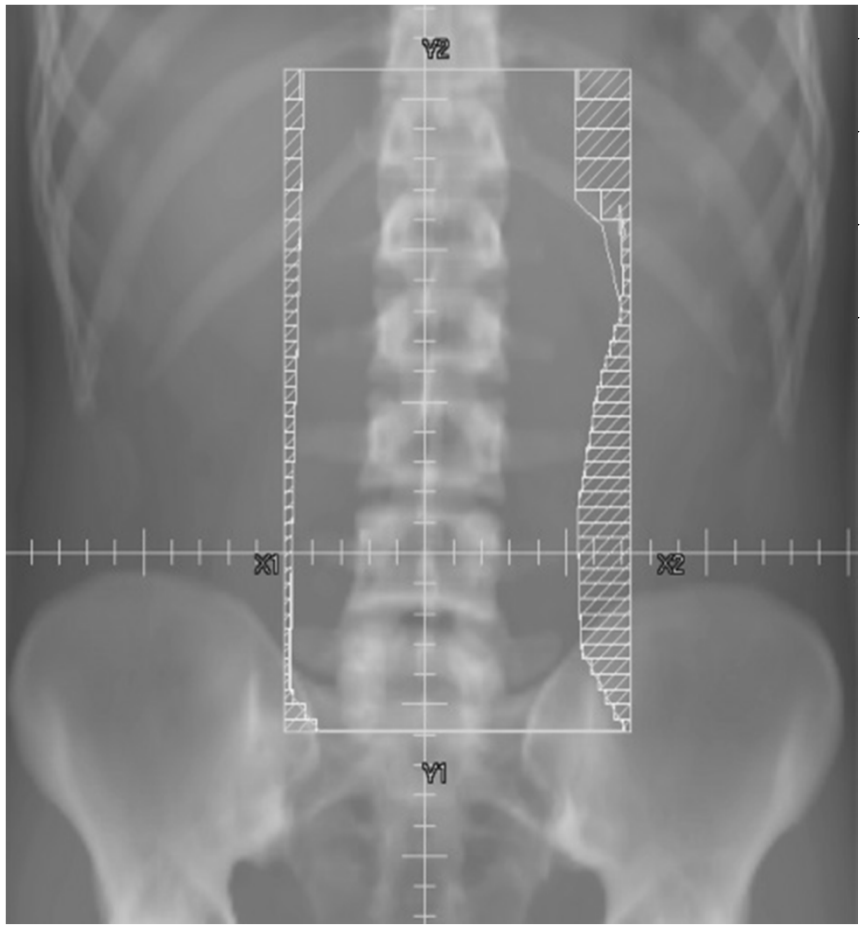
By S.D. Fosså, A. Horwich, J.M. Russell, J.T. Roberts, M.H. Cullen, N.J. Hodson, W.G. Jones, H. Yosef, G.M. Duchesne, J.R. Owen, E.J. Grosch, A.D. Chetiyawardana, N.S. Reed, B. Widmer, and S.P. Stenning for the Medical Research Council Testicular Tumor Working Party

- Between July 1989 and May 1993, 478 men with testicular seminoma stage I (T1 to T3) were randomized (PA- para-arotic strip: 236 patients; DL- dog leg field: 242 patients, 30 Gy/15 fractions/3 weeks)
- Median follow-up time is now 4.5 years.

	DL	PA
OS	100%	99.3%
RELAPSE FREE SURVIVAL 3YRS	96.6%	96%

- Acute toxicity (nausea, vomiting, leukopenia) was less frequent and less pronounced in patients in the PA arm. Within the first 18 months of follow-up, the sperm counts were significantly higher after PA than after DL irradiation.

CONVENTIONAL TECHNIQUE
STAGE I



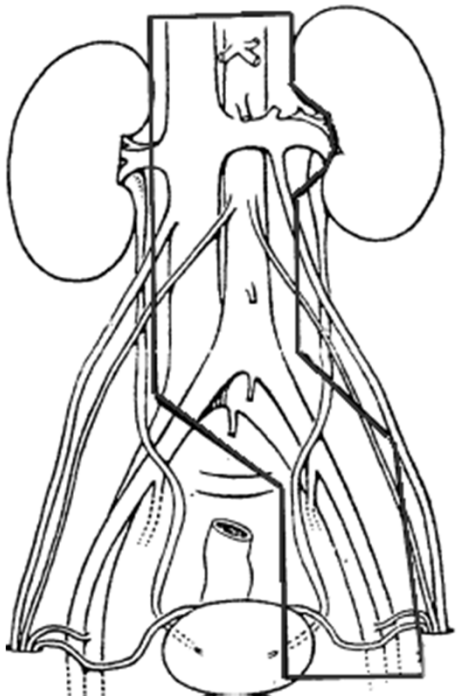
Superior: T10–T11 interspace

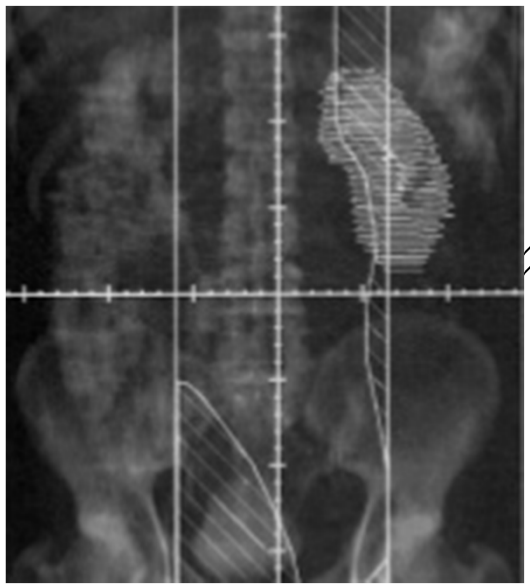
Inferior: L5–S1 interspace

Lateral: transverse process

For left testis: cover renal hilum

- **STAGE II**
- Superior: T10–T11 interspace
- Inferior: mid-obturator foramen
- Lateral: transverse process down to L5–S1 interspace, then diagonally to the lateral edge of the acetabulum, then vertically downward to the median border of the obturator foramen
- For left testis: cover renal hilum

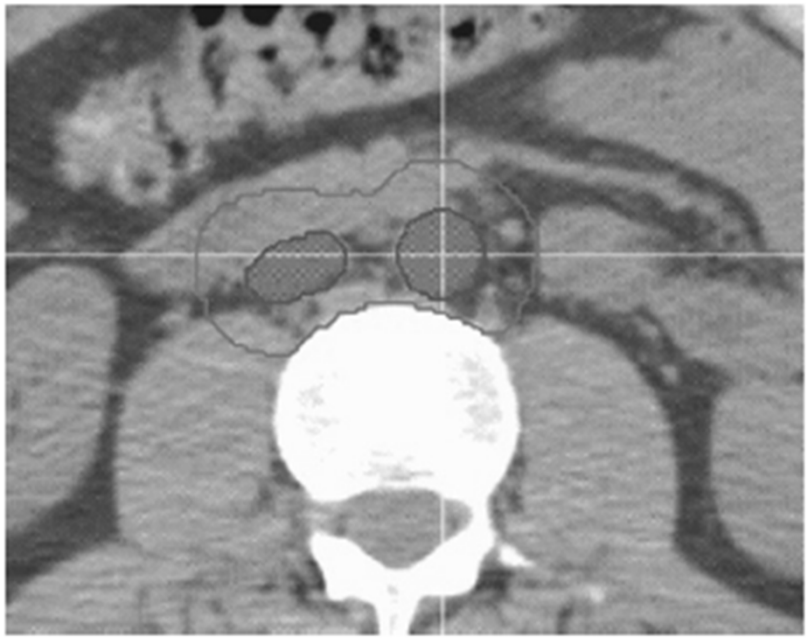




3DCRT-TECHNIQUE

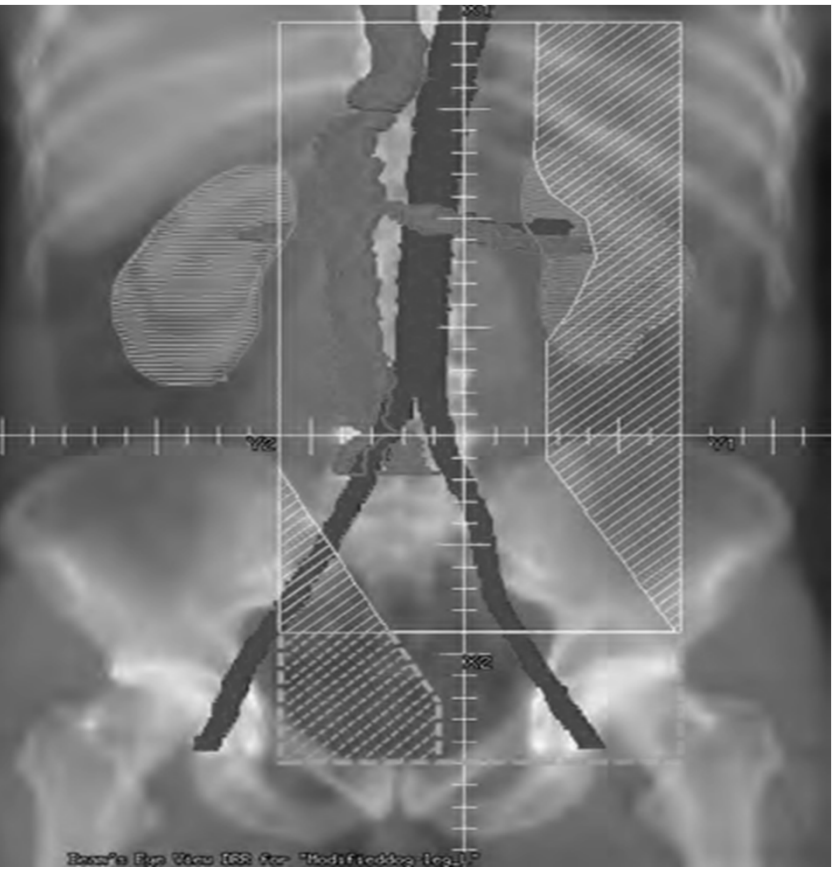
Position and immobilization	Supine with arms placed by the patient's side and legs straight. Immobilised with abdominopelvic orfit.
Slice thickness of CT	5 mm
Fiducials (mark)	Placed on the patient's skin laterally as well as anteriorly for alignment
Intravenous contrast	Administered to improve soft tissue and vascular definition

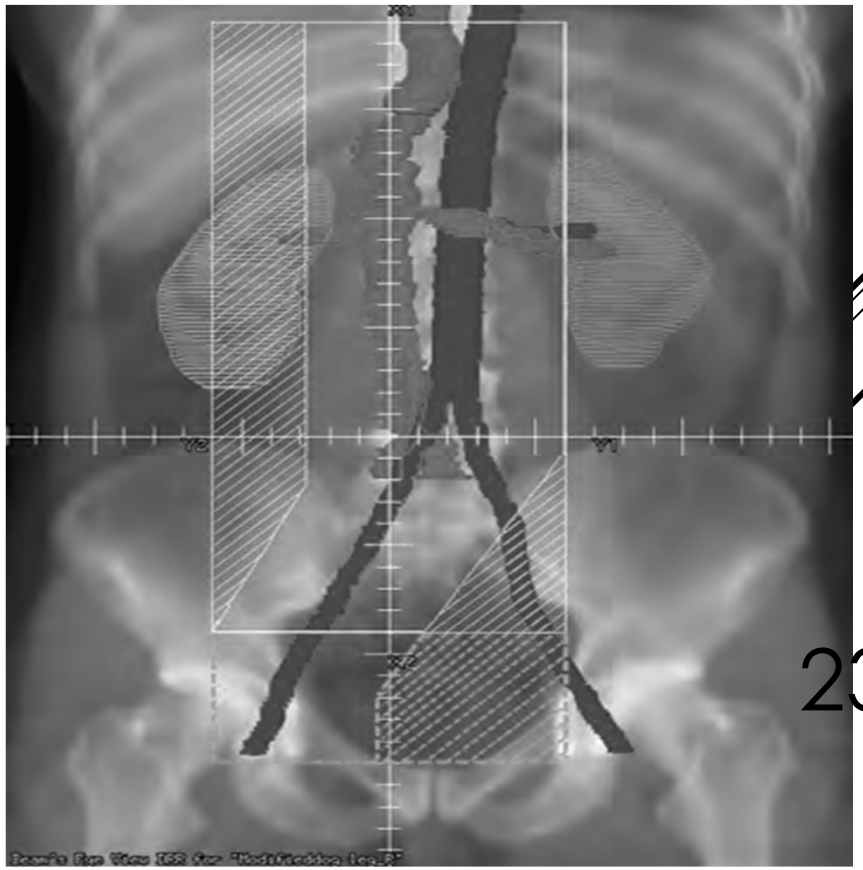
	CTV	TARGET VOLUME INCLUDES	DOSE
STAGE I	Begin at T10–T11 interspace, finish at aortic bifurcation. Contour aorta and vena cava together as vessel contour (VC) VC - 7 mm margin , excluding bones. For left testis: include renal hilum in CTV	Interaortocaval, preaortic, and para-aortic nodes.	20Gy in 10#
STAGE II	Begin at T10–T11 interspace, finish at obturator foramen. Contour aorta, vena cava and ipsilateral iliac nodes. VC -7 mm margin , excluding bones For left testis: include renal hilum. If gross tumor volume (nodal disease) - 1 cm margin, excluding bones.	Stage I target volume + ipsilateral pelvic nodes.	IIA-30 Gy in 15# IIB-36 Gy in 18#



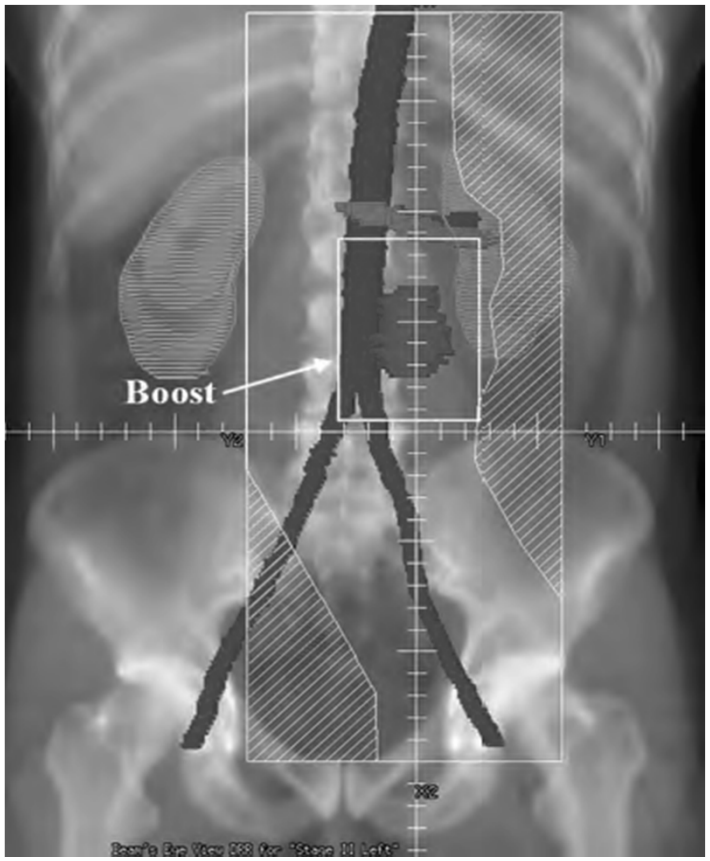
Clinical target volume (CTV) is generated by adding 7 mm to the contour of aorta and vena cava together as vessel contour (VC), with exclusion of bones.

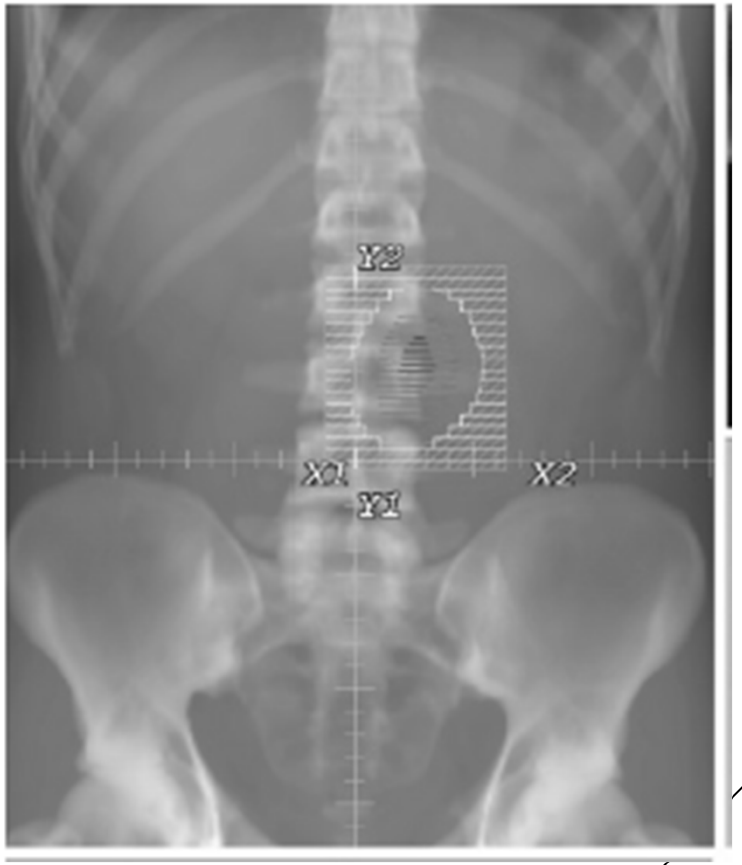
MODIFIED“DOG-LEG” FIELD IS USED TO ENCOMPASS NODAL REGIONS AT RISK. THE UPERIOR BORDER IS PLACED AT THE UPPER BORDER OF T 10 OR T 11 AND THE INFERIOR ORDER AT THE SUPERIOR ASPECT OF THE ACETABULUM. TRADITIONALLY, THE INFERIOR ORDER WAS PLACED AT THE SUPERIOR OBTURATOR FORAMEN (INDICATED IN *ORANGE)* O *INCLUDE ALL EXTERNAL ILIAC NODES*.
HESE NODES ARE RARELY INVOLVED, AND USING A HIGHER BORDER AS INDICATED WILL EDUCE TOXICITY





STAGE IIA AND STAGE II B SEMINOMA MAY BE TREATED WITH A TRADITIONAL OR MODIFIED DOG-LEG - BOOST OF 10 GY IN 5 FRACTIONS TO NODES >3 CM IN DIAMETER.





Inclusion of the inguinal scar, inguinal lymph nodes, or hemiscrotum is not routinely warranted.

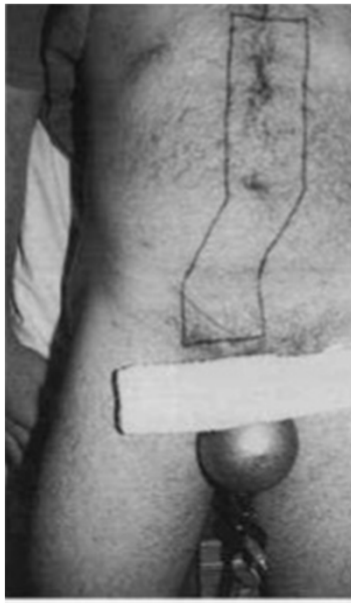
TESTICULAR SHIELDING

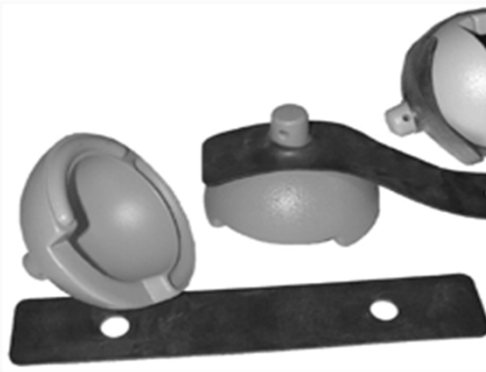
During a fractionated course of radiotherapy to the retroperitoneal and ipsilateral iliac lymph nodes, the dose to the remaining testis ranges between 0.3 and 1.5 Gy.

Dose received strongly depends on distance from the testicle to field edge.

Gonadal shielding, such as the clamshell device, which consists of a cup that is 1 cm thick (made of lead).

This shields the testicle from low-energy scattered photons and effectively reduces the testicular dose by a factor of 4.





- Treatment is delivered with a linear accelerator using anterior and posterior parallel opposed fields.
- Depending on the separation, 6- to 18-MV photons are utilized.
- Intensity-modulated radiotherapy (IMRT) to cover the target volume with greater sparing of organs at risk .

ORIGINAL ARTICLE

Bone marrow-sparing intensity-modulated radiation therapy for Stage I seminoma

THOMAS ZILLI, CHANTAL BOUDREAU, ROBERT DOUCET, MOEIN ALIZADEH, CAROLE LAMBERT, THU VAN NGUYEN & DANIEL TAUSSKY

Department of Radiation Oncology, CRCHUM - Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Hôpital Notre Dame, Montréal, Québec, Canada

Abstract

Background. A direct association between radiotherapy dose, side-effects and secondary cancers has been described in patients with seminoma. A treatment planning study was performed in order to compare computed tomography-based traditional radiotherapy (CT-tRT) versus bone marrow-sparing intensity-modulated radiation therapy (BMS-IMRT) in patients with Stage I seminoma. *Material and methods.* We optimized in 10 patients a CT-tRT and a BMS-IMRT treatment plan to deliver 20 Gy to the para-aortic nodes. CT-tRT and IMRT consisted of anteroposterior-posterioranterior parallel-opposed and seven non-opposed coplanar fields using 16 and 6-MV photon energies, respectively. Dose-Volume Histograms for clinical target volume (CTV), planning target volume (PTV) and organs at risk (OARs) were compared for both techniques using Wilcoxon matched-pair signed rank-test. *Results.* D_{mean} to CTV and PTV were similar for both techniques, even if CT-tRT showed a slightly improved target coverage in terms of PTV-$D_{95\%}$ (19.7 *vs.* 19.5 Gy, $p=0.005$) and PTV-$V_{95\%}$ (100 *vs.* 99.7%, $p=0.011$) compared to BMS-IMRT. BMS-IMRT resulted in a significant reduction (5.2 Gy, $p=0.005$) in the D_{mean} to the active bone marrow (ABM). The $V_{100\%}$ and $V_{75\%}$ of the OARs were reduced with BMS-IMRT by: ABM-$V_{100\%}$=51.7% and ABM-$V_{75\%}$=42.3%; bowel-$V_{100\%}$=15.7% and bowel-$V_{75\%}$=16.8%; stomach-$V_{100\%}$=22% and stomach-$V_{75\%}$=27.7%; pancreas-$V_{100\%}$=37.1% and pancreas-$V_{75\%}$=35.9% ($p=0.005$ for all variables). *Conclusions.* BMS-IMRT reduces markedly the dose to the OARs compared to CT-tRT. This should translate into a reduction in acute and long-term toxicity, as well as into the risk of secondary solid and hematological cancers.

Table I. Target volume and organs at risk dose constraints used in bone marrow-sparing intensity-modulated radiotherapy treatment planning.

Structure	Constraints	Volume (%)	Dose in Gy (%)
CTV	Upper	0	22 (110%)
	D_{mean}	100	20 (100%)
PTV	Upper	1	21.4 (107%)
	Lower	100	19 (95%)
ABM	D_{mean}	100	< 7.5
Combined kidneys	Upper	1	20 (100%)
	Upper	20	15 (75%)
	Upper	33	10 (50%)
	D_{mean}	100	< 6.9
Bowel	Upper	50	10 (50%)
Stomach	Upper	50	5 (25%)
Pancreas	Upper	30	20 (100%)
	Upper	50	15 (75%)
Liver	Upper	33	10 (50%)
Spinal cord	No dose constraint		

CTV, clinical target volume; PTV, planning target volume; ABM, active bone marrow.

Table III. Comparison of dosimetric parameters for organs at risk and non-target tissues. Results in mean ± SD (n = 10).

Variable	CT-tRT	BMS-IMRT	p-value
Active bone marrow			
D_{mean} (Gy)	13.1 ± 1.3	7.9 ± 0.5	0.005*
$D_{50\%}$ (Gy)	19.7 ± 1.2	7.1 ± 0.9	0.005*
$V_{100\%}$ (%)	53.4 ± 5.9	1.7 ± 0.8	0.005*
$V_{75\%}$ (%)	59.0 ± 5.9	16.7 ± 1.4	0.005*
$V_{50\%}$ (%)	61.2 ± 5.9	34.9 ± 3.2	0.005*
Combined kidneys			
D_{mean} (Gy)	6.8 ± 1.5	8.0 ± 0.8	0.007*
$D_{50\%}$ (Gy)	2.2 ± 1.3	7.4 ± 0.9	0.005*
$V_{100\%}$ (%)	8.6 ± 4.0	0.9 ± 0.4	0.005*
$V_{75\%}$ (%)	25.1 ± 6.8	8.8 ± 2.5	0.005*
$V_{50\%}$ (%)	30.4 ± 8.0	23.9 ± 7.1	0.038*
Bowel			
D_{mean} (Gy)	6.2 ± 1.0	8.1 ± 0.7	0.005*
$D_{50\%}$ (Gy)	0.9 ± 0.3	8 ± 0.4	0.005*
$V_{100\%}$ (%)	17.2 ± 4.6	1.5 ± 0.8	0.005*
$V_{75\%}$ (%)	24.7 ± 4.6	7.9 ± 2.5	0.005*
$V_{50\%}$ (%)	27.3 ± 4.9	26.6 ± 5.6	0.959
Stomach			
D_{mean} (Gy)	7.6 ± 3.8	5.0 ± 2.3	0.011*
$D_{50\%}$ (Gy)	5.0 ± 7.2	3.4 ± 2.6	0.878
$V_{100\%}$ (%)	22.4 ± 13.0	0.4 ± 1.0	0.005*
$V_{75\%}$ (%)	30.8 ± 17.7	3.1 ± 3.0	0.005*
$V_{50\%}$ (%)	33.8 ± 19.2	14.9 ± 8.3	0.005*
Pancreas			
D_{mean} (Gy)	12.5 ± 3.6	12.2 ± 1.7	0.799
$D_{50\%}$ (Gy)	16.3 ± 5.7	10.2 ± 3.7	0.017*
$V_{100\%}$ (%)	40.2 ± 16.4	3.1 ± 3.7	0.005*
$V_{75\%}$ (%)	61.5 ± 17.6	25.6 ± 14.4	0.005*
$V_{50\%}$ (%)	65.3 ± 16.5	62.8 ± 14.2	0.575
Liver			
D_{mean} (Gy)	2.8 ± 1.6	3.8 ± 1.3	0.008*
$D_{50\%}$ (Gy)	0.4 ± 0.1	2.3 ± 1.6	0.005*
$V_{100\%}$ (%)	3.2 ± 3.5	0.1 ± 0.3	0.018*
$V_{75\%}$ (%)	8.0 ± 6.0	1.9 ± 1.3	0.008*
$V_{50\%}$ (%)	10.0 ± 6.9	8.4 ± 4.7	0.173
Spinal Cord			
D_{max} (%)	107.4 ± 1.7	65.7 ± 5.0	0.005*
D_{mean} (Gy)	19.8 ± 0.5	8.0 ± 0.8	0.005*
$D_{50\%}$ (Gy)	21.0 ± 0.3	8.5 ± 0.7	0.005*
Non-target tissues			
$Dose_{Int}$	1.02 ± 0.18	0.99 ± 0.20	0.028*

DOSE CONSTRAINTS (Quantec data)

Structure	Volume	Dose	Toxicity rate	Toxicity end point
Kidney, bilateral	Mean	<15-18 Gy	<5%	Clinical dysfunction
Kidney, bilateral	Mean	<28 Gy	<50%	Clinical dysfunction
Kidney, bilateral	V12	<55%	<5%	Clinical dysfunction
Kidney, bilateral	V20	<32%	<5%	Clinical dysfunction
Kidney, bilateral	V28	<20%	<5%	Clinical dysfunction

Table 2 Clinical Stage I Seminoma: Surveillance after Adjuvant Treatment (Chemotherapy or Radiati

	Year (at month intervals)				
	1	2	3	4	5
H&P[1,2]	Every 6–12 mo	Every 6–12 mo	Annually	Annually	Annually
Abdominal/ Pelvic CT	Annually	Annually	Annually	------	
Chest x-ray	As clinically indicated, consider chest CT in symptomatic patients.				

- SALVAGE RT
- Patients with stage II or III disease post treatment may present with residual masses.
- Flechon et al.reported that 50% of residual masses disappeared on follow-up, and viable cancer cells were found only in masses >3 cm in size.
- Observation alone is adequate for a residual mass <3 cm in size.
- In cases with residual disease > 3cm Salvage RT or surgical resection can be considered.

- PALLIATIVE RT-
- To be considered in metastatic disease to the involved site.

NCCN GUIDELINES

Stage	Treatment
STAGE IA, IB	Surveillance(pT1-pT3) OR Single agent carboplatin – AUC-7x 1or 2 cycles OR RT-20Gy/10#
STAGE IS	Repeat serum tumor markers and abdominal CT – look for disease.
STAGE IIA	RT-Irradiation of the para-aortic and ipsilateral pelvic nodes to 30Gy (preferred) OR Primary chemotherapy- EPx 4 cycles or BEPx 3 cycles
STAGEIIB	Primary chemotherapy- EPx 4 cycles or BEPx 3 cycles (preferred)OR RT-Irradiation in select non bulky cases - para-aortic and ipsilateral pelvic nodes to 36Gy

BILATERAL TESTICULAR TUMOR

- Bilateral Orchidectomy .
- Organ sparing surgery (for tumors involving <30% of testicular volume) to preserve hormonal function followed by low dose radiation therapy (16-20 Gy) using direct fields with electron to remaining testis.
- Adjuvant radiation therapy may be postponed if fertility is an issue, but requires follow up.

GCT WITH HORSESHOE KIDNEY

- 1/400 persons in general public.
- Standard dose causes radiation nephritis.
- Large portion of kidney overlies lymph nodes.
- Post orchidectomy :
  - Stage I : Surveillance.
  - Stage II : chemotherapy.
- Retroperitoneal lymph node dissection is an alternative; if patients unwilling for surveillance (safe and effective).

- **In immunocompromise-HIV infected men there is increase risk of testicular cancer**
- Offered same treatment as standard oncologic therapy.

SPERM BANKING

- **Sperm quality may be poor before starting therapy.**

- **Many patients have to start chemotherapy immediately or soon enough to limit the number of ejaculates to one or two samples.**

- **Recent progress in andrology and use of assisted reproductive technique (Intracytoplasmic sperm injection) allows freezing and future use of very limited amount of sperm .**

SEQUELAE OF RT

- **IMPAIRED SPERMATOGENESIS**

- Approximately 50% of patients with testicular seminoma have some degree of impairment in spermatogenesis at the time of presentation.

- Exposure of the remaining testis to therapeutic irradiation may further impair fertility, and the degree of impairment is dose dependent.

- Hormonal function and spermatogenesis may be compromised at dose levels as low as 0.5 Gy and that cumulative doses >2 Gy probably lead to permanent injury.

Assessment of fertility and sexual function was performed in the Southwest Oncology Group Study 8711 in a series of men following orchidectomy and radiotherapy.

54% were sub fertile at baseline, with a sperm count <20,000/mL. The average

prescribed dose was 26 Gy @ 1.6-Gy per fractions, delivering a median dose of 79 cGy to t remaining testis.

The sperm count tended to drop to a nadir value around 6 months, with recovery of fertility by 12 months.

With higher testicular dose, recovery of sperm count was further delayed.

Dog-leg radiotherapy also results in an elevation of serum follicle-stimulating hormone (FSH levels, with no change in serum testosterone.

FSH levels are highest within 6 months of radiotherapy and return to normal within 3 years.

Radiation senstivity	Spermatogonia (~0.1–0.2 Gy) Spermatocytes (~2–3 Gy) Spermatids (~4–6 Gy) Azospermia takes approximately 60–70 days after a single dose below 2 Gy, due to damage to spermatogonia, but develops faster in case of RT> 4 Gy, due to concurrent damage to spermatids
Recovery	Sperm recovery: 1–1.5 years for <1 Gy, 2–5 years for 4–6 Gy Mostly permanent azospermia for 6–8 Gy
FSH	Dose of 0.75–6 Gy might cause an increase in FSH
LH	0.75 Gy might increase LH levels through loss of negative feedback

▸ SECOND MALIGNANCY

- Patients are at increased risk of developing a second primary malignancy following treatment for testicular cancer.

- Travis et al. investigated the occurrence of second malignancies among >40,000 men who had undergone treatment for testicular cancer (14 population based cancer registries in North America and Europe).

- The risk of developing a second solid tumor among 10-year survivors was almost twice that of the general population, with a relative risk (RR) of 1.9.

- **The highest risk for cancers of the stomach (RR 4.0), pancreas (RR 3.6), and bladder (RR 2.7).**

- Patients treated with radiotherapy alone (RR 2.0), chemotherapy alone (RR 1.8), and both modalities (RR 2.9).
- An increased rate of spontaneous chromosomal translocations is seen in lymphocytes of patients with early-stage seminoma compared to healthy controls.
- Following adjuvant radiotherapy, the translocation rate increases before returning to pre radiotherapy levels at around 30 months.
- It is hypothesized that this genomic instability may be a predisposing factor toward malignancy development.

THANK YOU