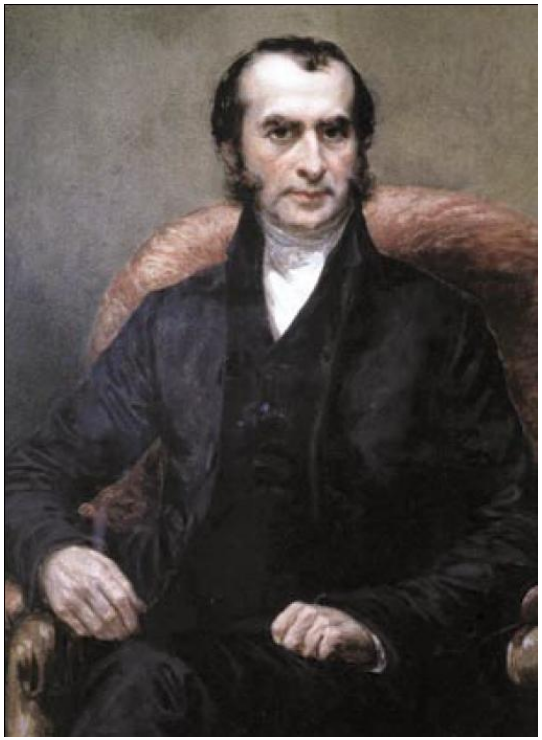
Àrea Integral
de Salut
Barcelona Esquerra

III Jornada d'Atenció Compartida en Oncologia i Hematologia Àrea Integral de Salut Barcelona Esquerra

MALALTIA DE HODGKIN
HISTÒRIA I TOXICITAT

Joan C. JULIÀ
Cap Clínic. HOSPITAL PLATÓ
Barcelona, 21 de Març de 2014

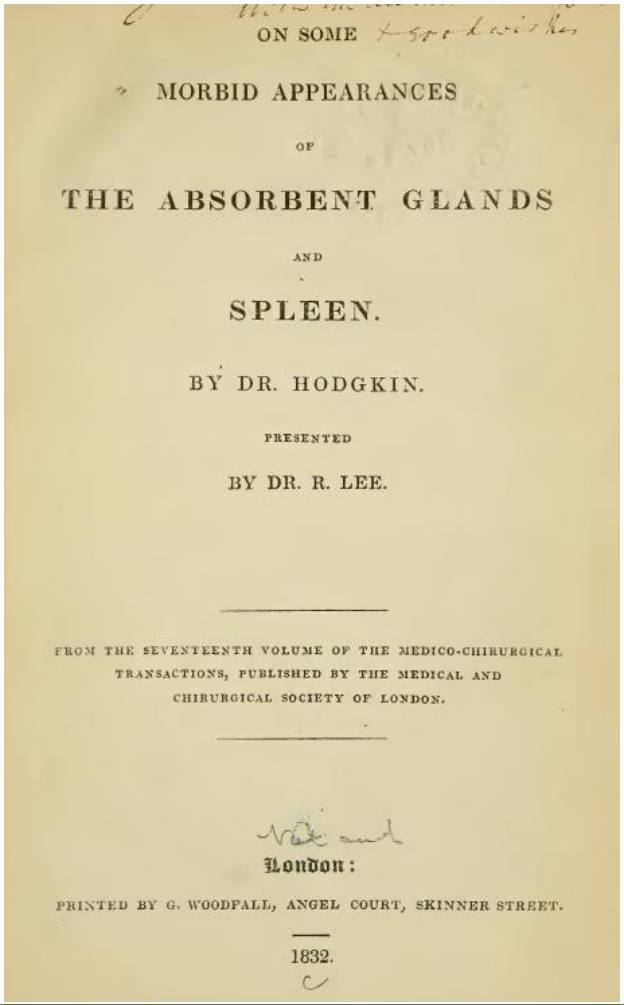


THOMAS HODGKIN
1798 - 1866

EL 1826 GUY'S HOSPITAL (LONDRES).

"INSPECTOR OF THE DEAD"

"CURATOR OF THE MUSEUM OF MORBID ANATOMY"



ON SOME

MORBID APPEARANCES

OF

THE ABSORBENT GLANDS

AND

SPLEEN.

BY DR. HODGKIN.

PRESENTED

BY DR. R. LEE.

FROM THE SEVENTEENTH VOLUME OF THE MEDICO-CHIRURGICAL TRANSACTIONS, PUBLISHED BY THE MEDICAL AND CHIRURGICAL SOCIETY OF LONDON.

London:

PRINTED BY G. WOODFALL, ANGEL COURT, SKINNER STREET.

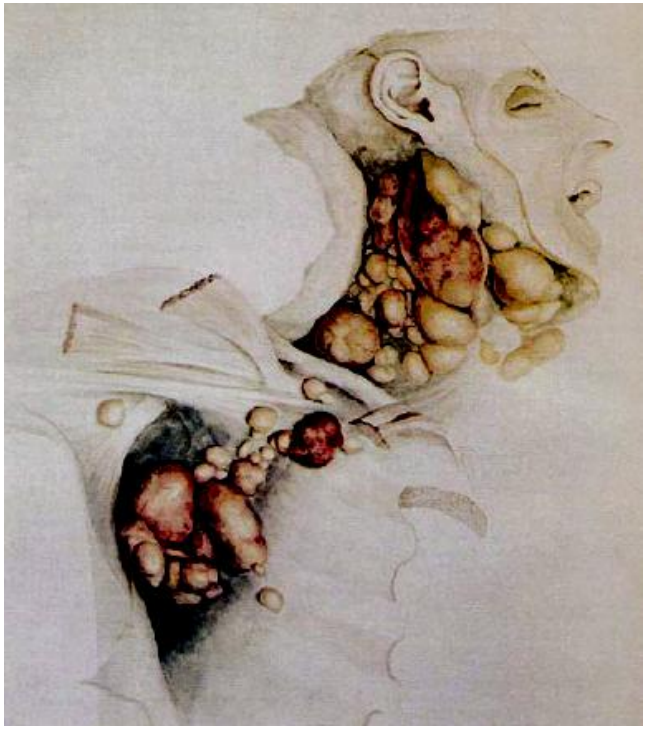
1832.

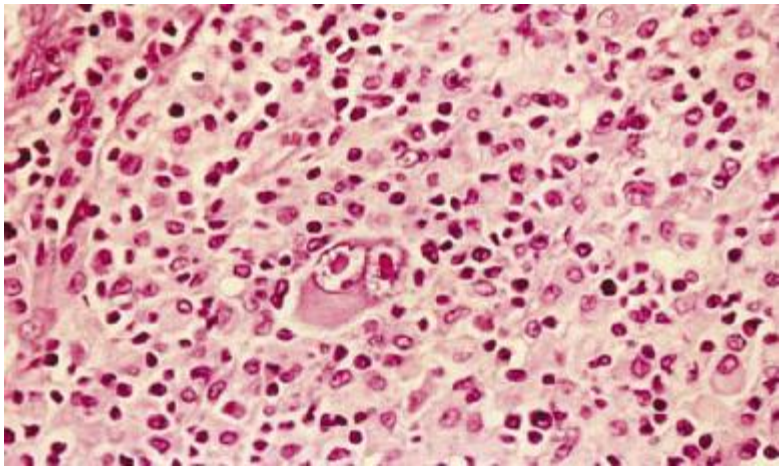
DR. HODGKIN ON SOME MORBID APPEARANCES OF THE ABSORBENT GLANDS AND SPLEEN.

CASE II.

September 24, 1828. Ellenborough King, aged ten years, was admitted into Luke's ward on the 6th of

That as far as could be ascertained from observation, or from what could be collected from the history of the cases, this enlargement of the glands appeared to be a primitive affection of those bodies, rather than the result of an irritation propagated to them from some ulcerated surface or other inflamed texture





1865

CASES OF

ENLARGEMENT OF THE LYMPHATIC GLANDS AND SPLEEN,

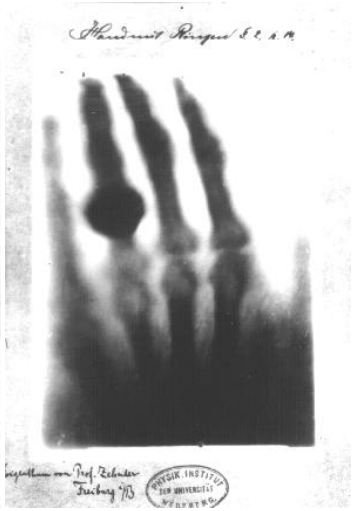
(OR, HODGKIN'S DISEASE,)

WITH REMARKS.

By SAMUEL WILKS, M.D.

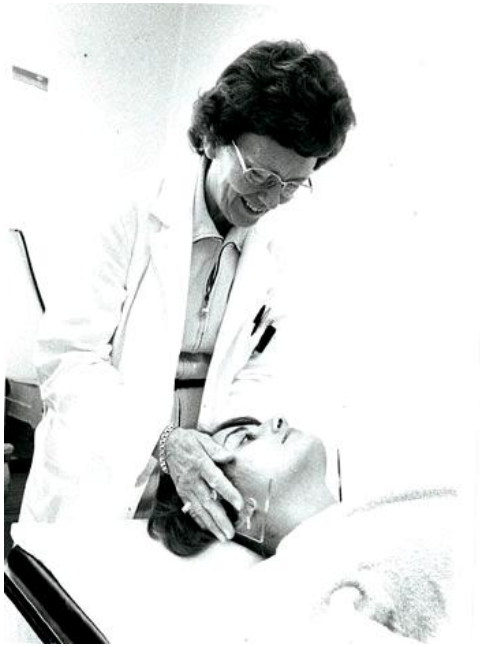
Having spoken of the lardaceous affection, I must now call

1895

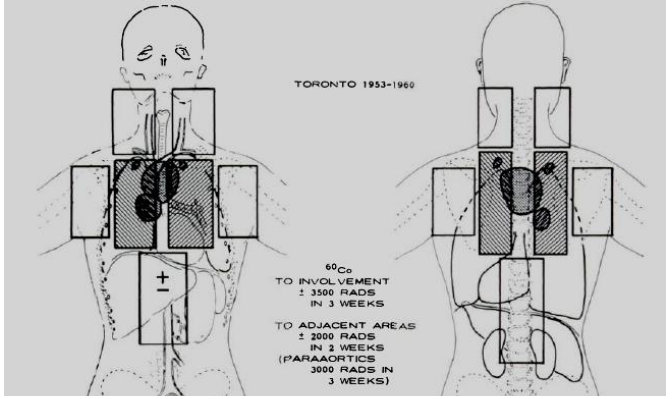


_1902_ PUSEY WA. CASES OF SARCOMA AND HODGKIN'S DISEASE TREATED BY EXPOSURE TO X-RAYS A PRELIMINARY REPORT. J Am Med Assoc 1902;38 166-96

_1939_ GILBERT Renè. RADIOTHERPAY IN HODKIN'S DISEASE (MALIGNANT GRANULOMATOSIS).ANATOMICAL CLINICAL FOUNDATIONS; GOVERNING PRINCIPES ; RESULTS. Am J Roentgenol Radium Ther 1939;44 :198-241.



VERA PETERS
1911 - 1993



Peters MV. A study of survivals in Hodgkin's disease treated radiologically. *Am J Roentgenol Radium Ther* 1950;63:299–311.

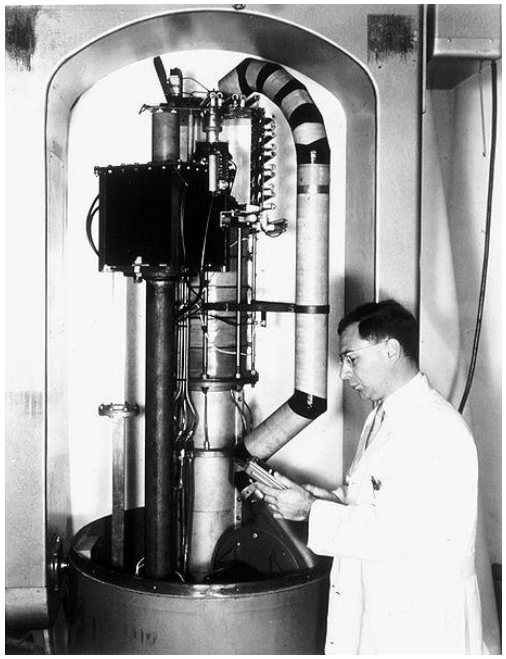
Peters MV, Middlemiss KC. A study of Hodgkin's disease treated by irradiation. *Am J Roentgenol Radium Ther Nucl Med* 1958;79:114–21.

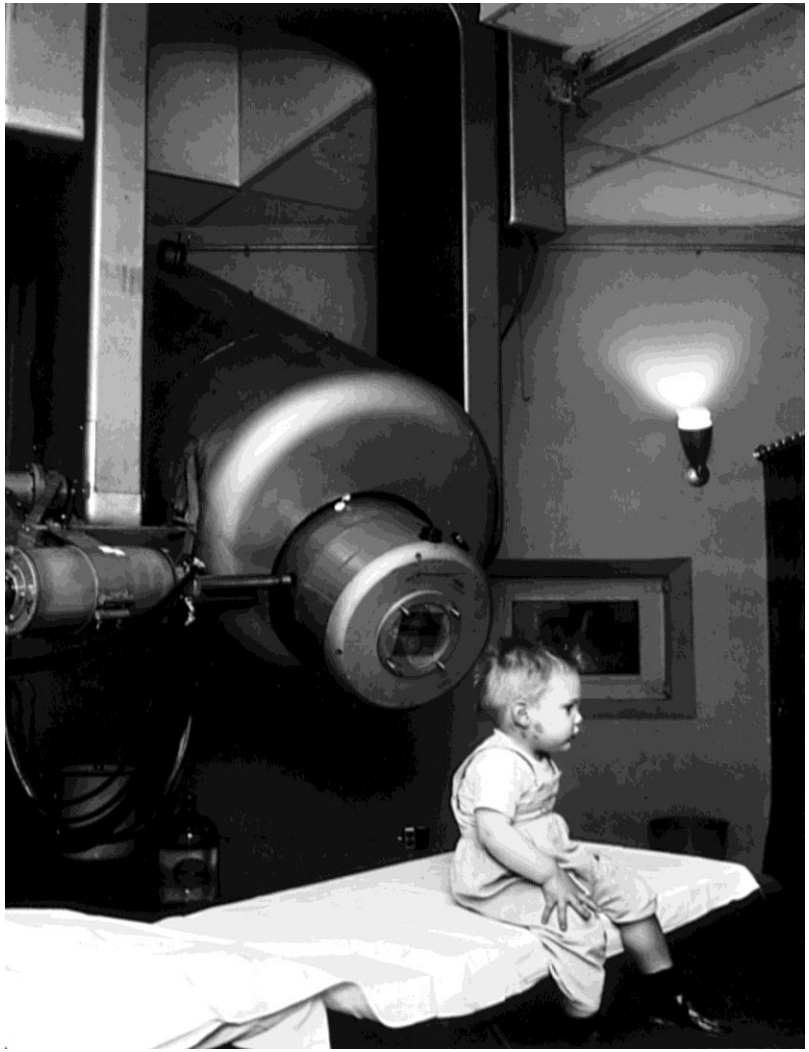
Peters MV. The need for a new clinical classification in Hodgkin's disease: keynote address. *Cancer Res* 1971;31:1713–22.

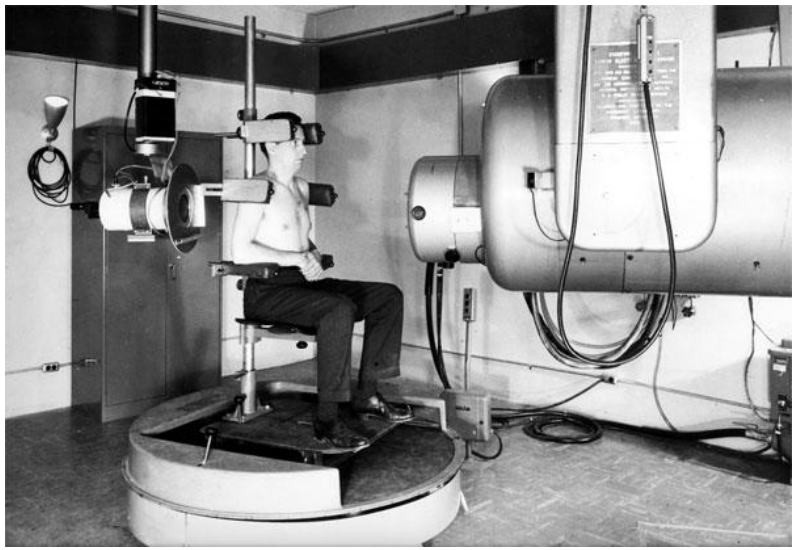
Peters MV, Brown TC, Rideout DF. Updated Hodgkin's disease: B. Curability of localized disease. Prognostic influences and radiation therapy according to pattern of disease. *JAMA* 1973;223:53–9.

Peters MV. Prophylactic treatment of adjacent areas in Hodgkin's disease. *Cancer Res* 1966;26:1232–43.

HENRY KAPLAN
1918 - 1984







Cancer Research

Extended-Field Radical Radiotherapy in Advanced Hodgkin's Disease: Short-Term Results of 2 Randomized Clinical Trials

Henry S. Kaplan and Saul A. Rosenberg

Cancer Res 1966;26:1268-1276.

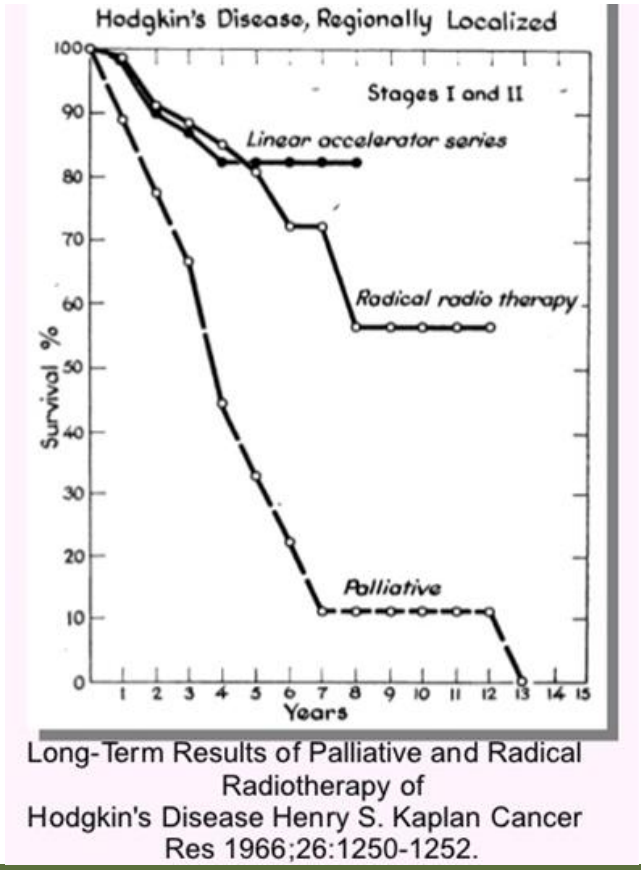
ROLE OF INTENSIVE RADIOTHERAPY IN THE MANAGEMENT OF HODGKIN'S DISEASE

HENRY S. KAPLAN, MD

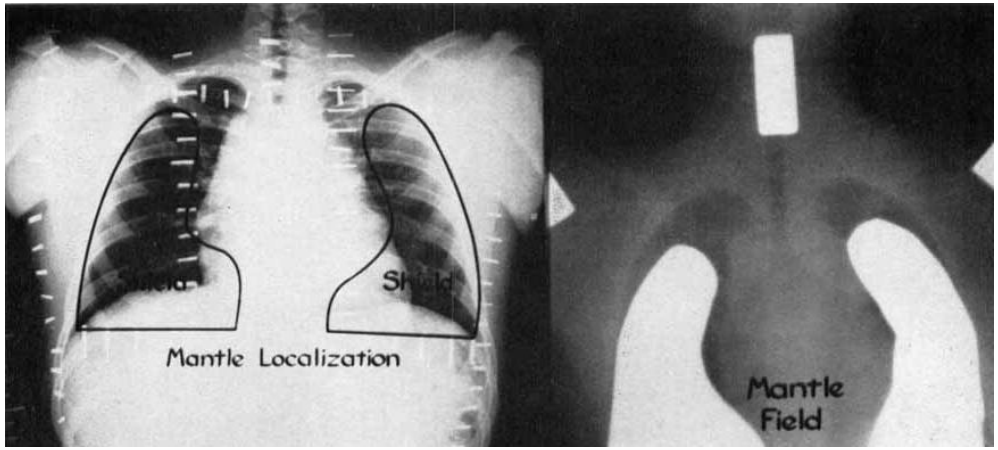
CONCLUSIONS

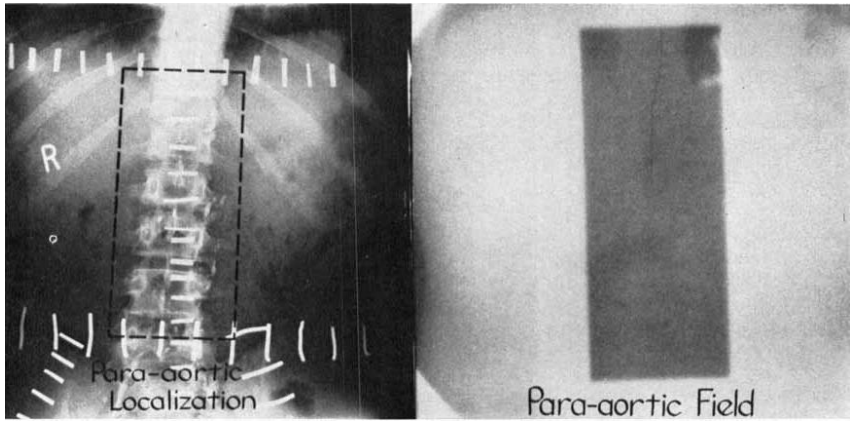
It is concluded that arguments supporting the pessimistic position that Hodgkin's disease is always incurable are no longer valid. There is mounting evidence to support the use of the term "cure" and to indicate that an appreciable number of patients with Hodgkin's disease have been cured.

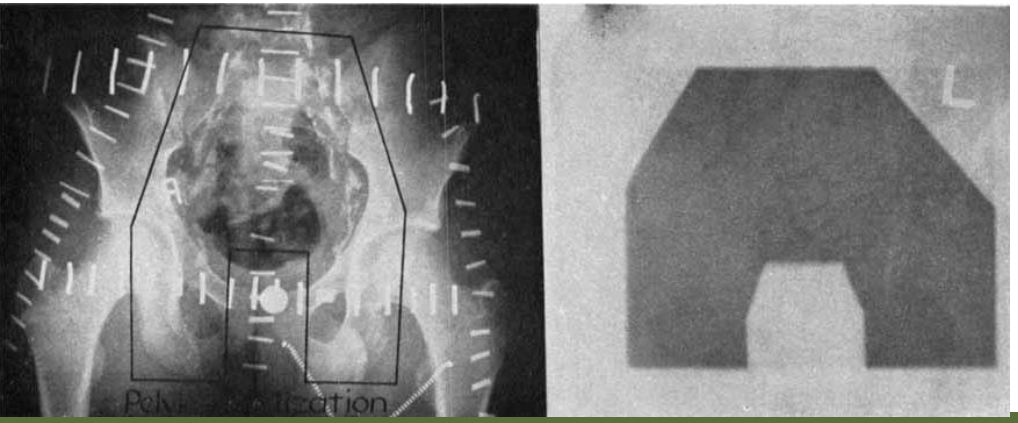
Megavoltage radiotherapy to doses of 3,500 to 4,000 rads in approximately 4 weeks over wide fields covering the involved lymph node chains in continuity is the treatment of choice for regionally localized disease and offers a substantial chance of permanent cure.



Long-Term Results of Palliative and Radical Radiotherapy of Hodgkin's Disease Henry S. Kaplan Cancer Res 1966;26:1250-1252.







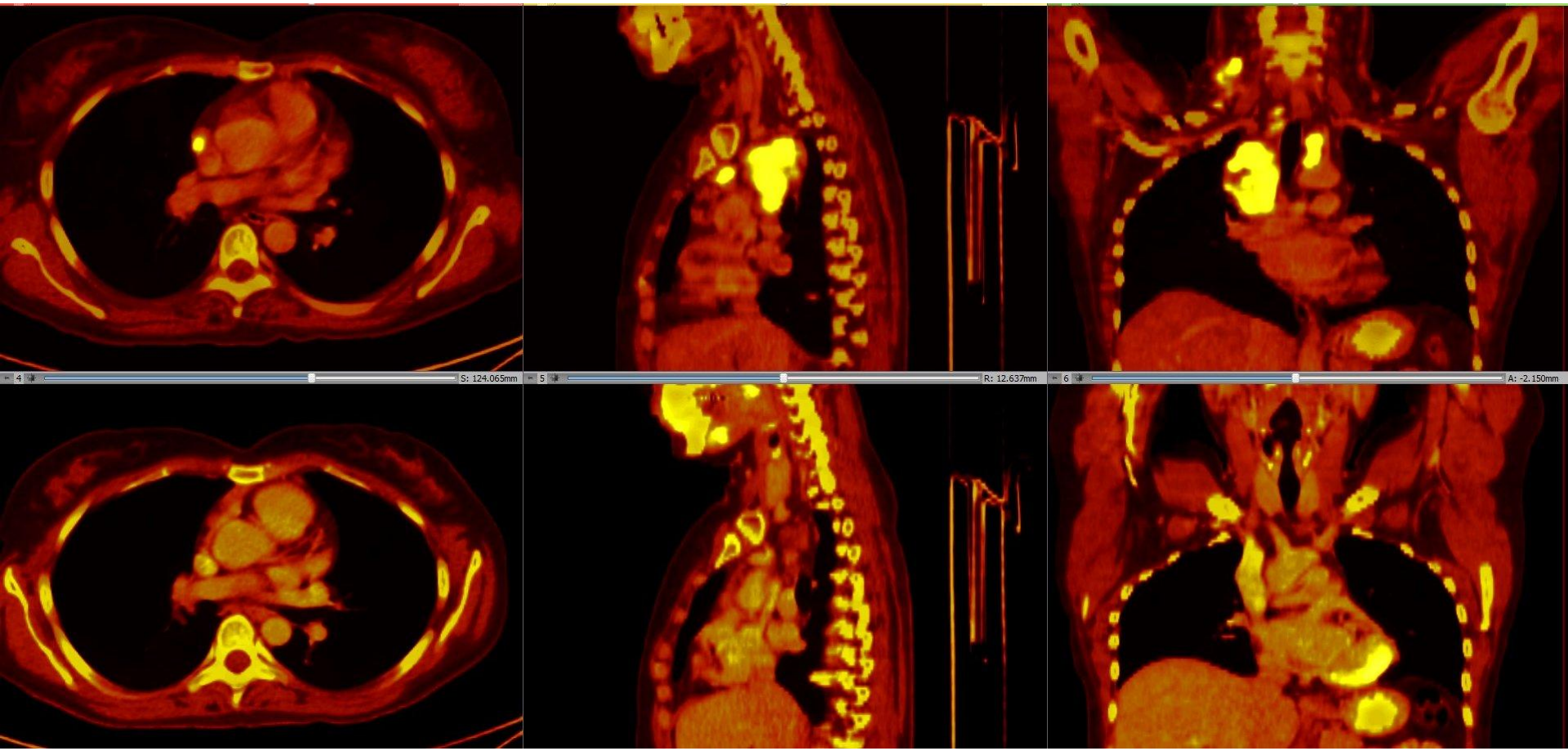
CAMPS EXTENSOS

DOSIS ALTES

TOXICITAT TARDANA ASSOCIADA A RT

- ***DOSI D'IRRADIACIÓ***
- ***ÀREA IRRADIADA***
- ***EDAT EN LA QUE ES VA SER TRACTAT***

- ***SEGONS CÀNCERS***
- ***MALALTIA CARDÍACA***
- ***DISFUNCIONS ENDOCRINES (TIROIDES)***


4
S: 124.065mm
5
R: 12.637mm
6
A: -2.150mm

CAMP EXTENS

1945.5 cc

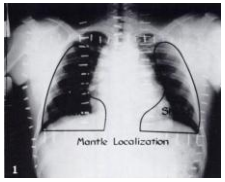
DOSI 30- 46Gy

ENERGIA 1.4 MV

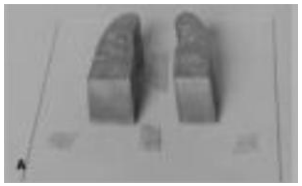
PLANIFICACIÓ

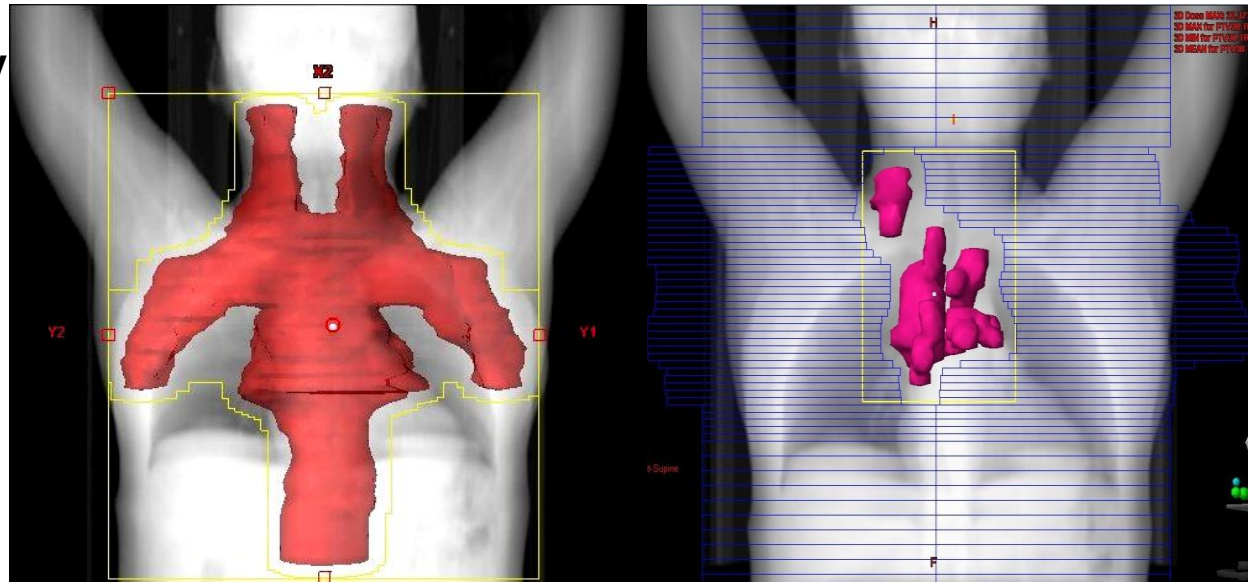
2D

SIMULADORS / RX



MOTLLOS





CAMP AFECTAT

180.5 cc

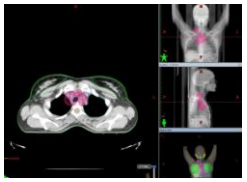
DOSI 20- 30Gy

ENERGIA 6-18 MV

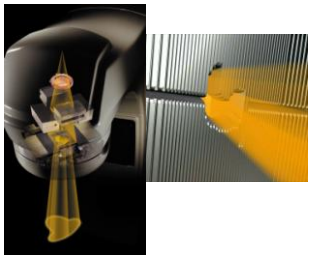
PLANIFICACIÓ

3D

TAC + FUSIÓ



MLC



CONE VIEW

TOMO TERÀPIA

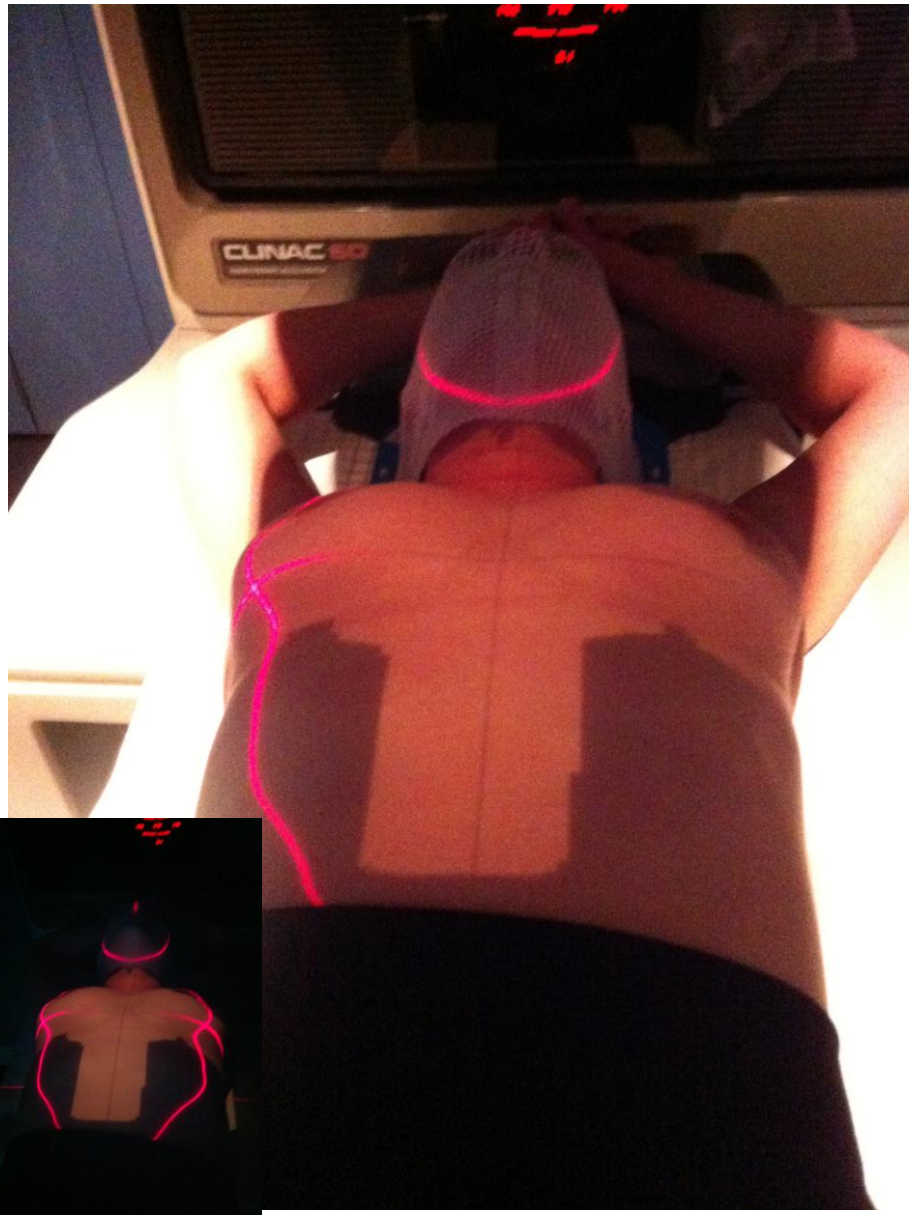
IMRT

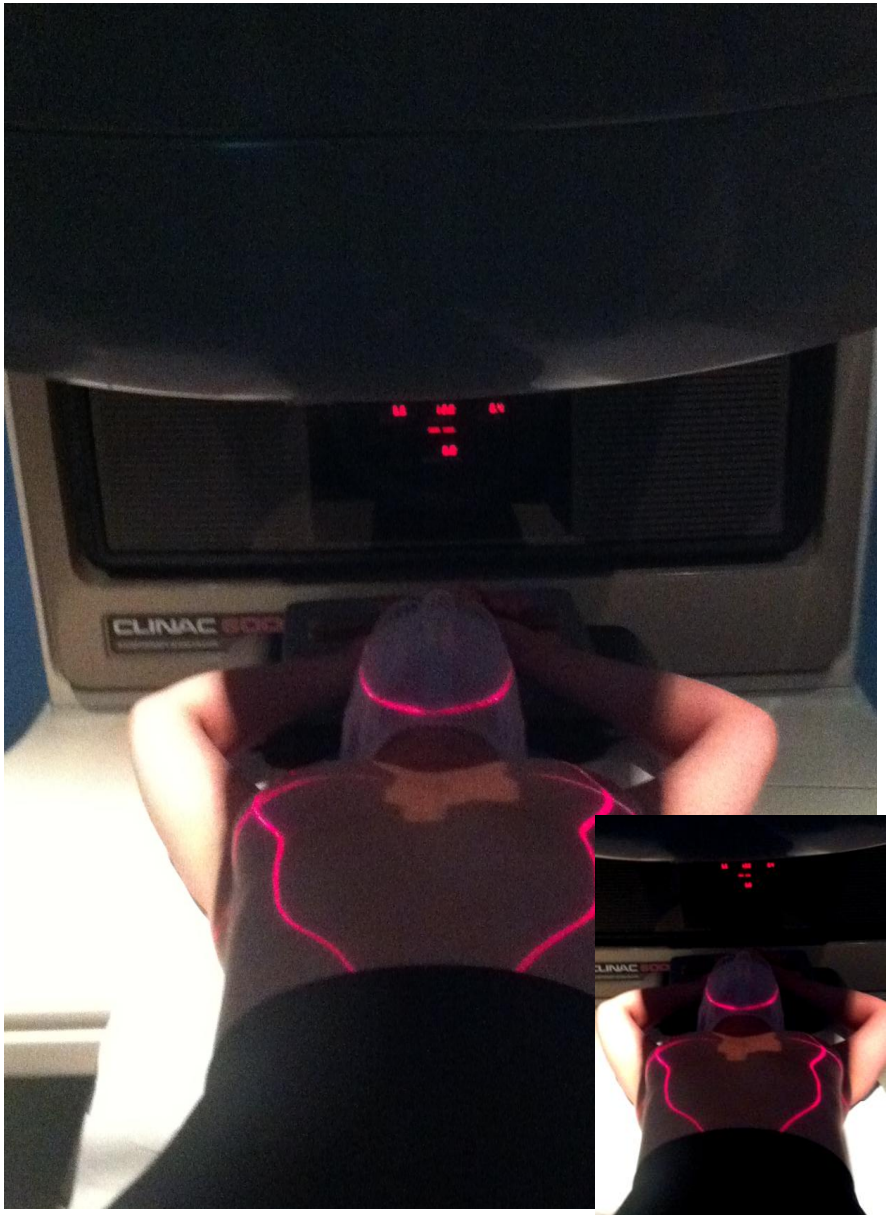
VERIFICACIÓ

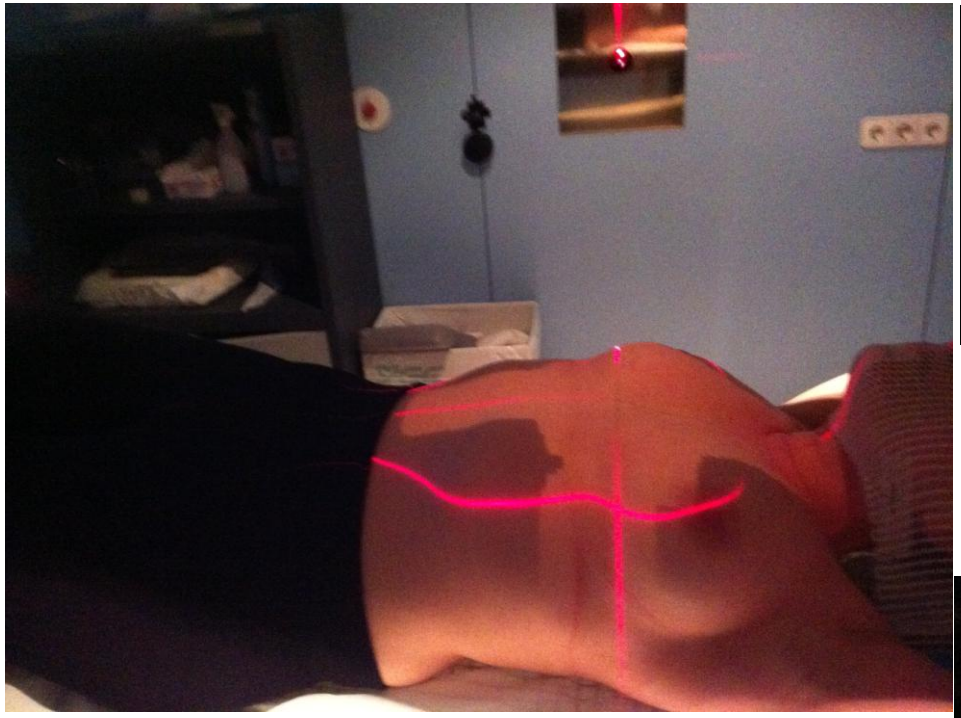
POSICIONAMENT

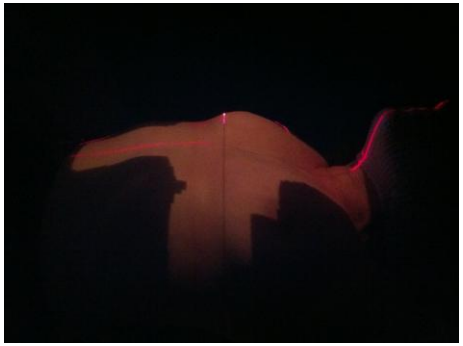
RT GUIADA PER

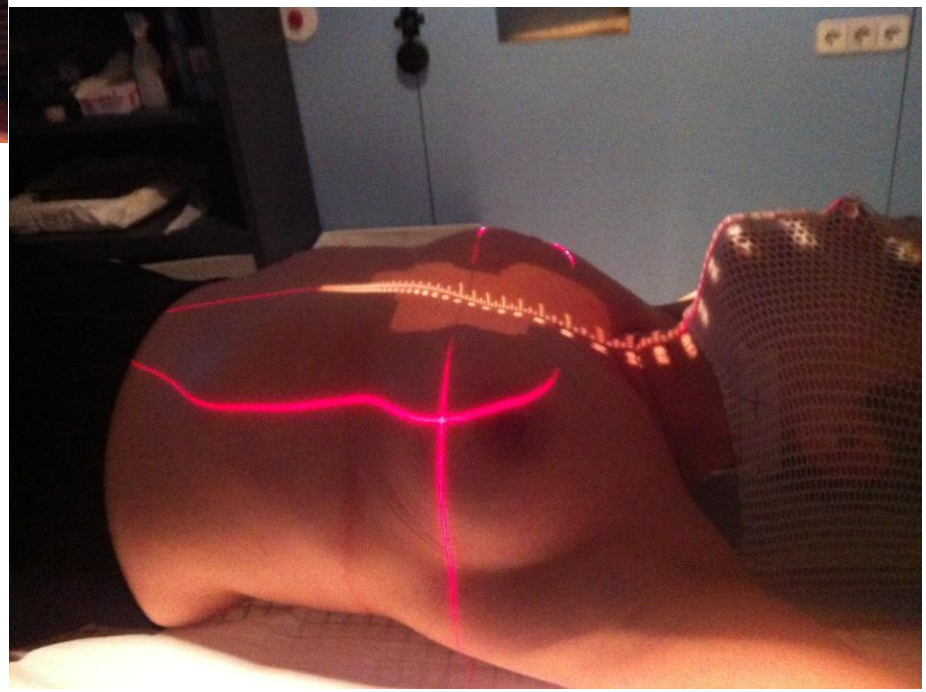
IMATGE

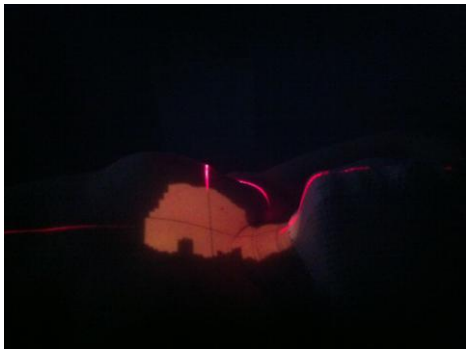

CLINAC


CLINAC









SEGONS CÀNCERS

LA MAJOR CAUSA DE MORBIDITAT I MORTALITAT DELS SUPERV.

LA MAJORIA SON TUMORS SÒLIDS (60/1)

LATÈNCIA DE 5 A 10 ANYS

VOLUME 25 · NUMBER 12 · APRIL 20 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Long-Term Solid Cancer Risk Among 5-Year Survivors of Hodgkin's Lymphoma

David C. Hodgson, Ethel S. Gilbert, Graça M. Dores, Sara J. Schonfeld, Charles F. Lynch, Hans Storm, Per Hall, Froydis Langmark, Eero Pukkala, Michael Andersson, Magnus Kaijser, Heikki Joensuu, Sophie D. Fossâ, and Lois B. Travis

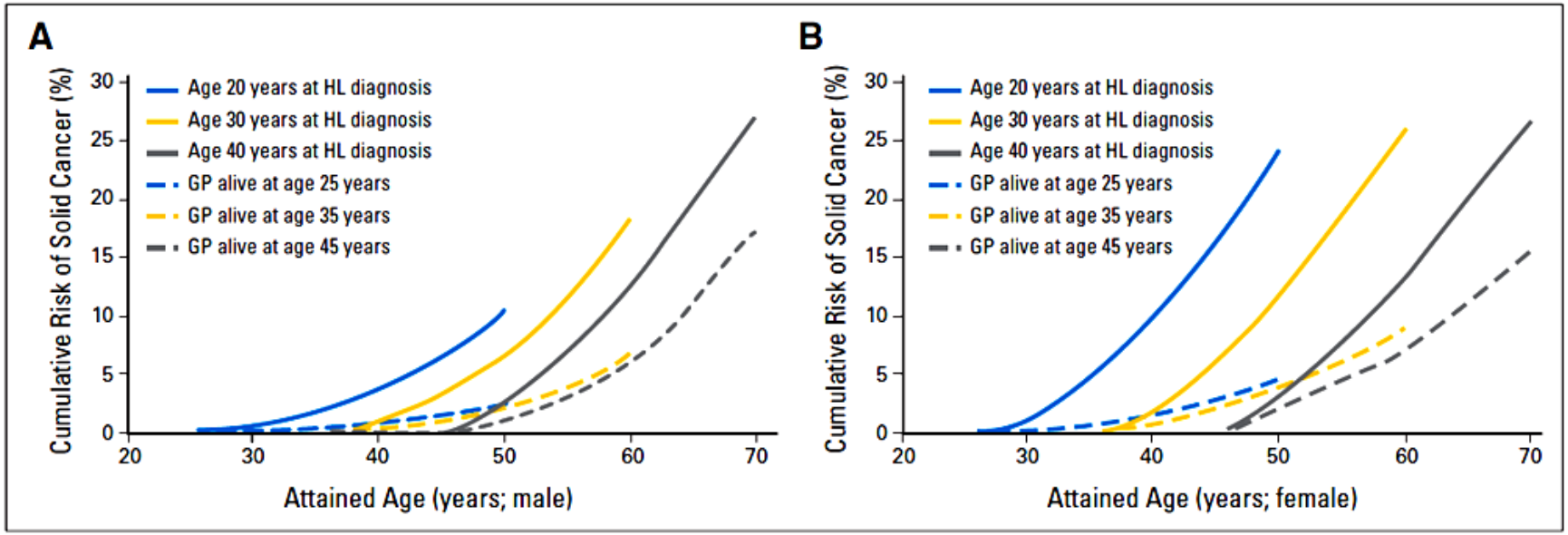
18.862 SUPERVIVIENTS. (1970 – 2001). EDAT MITJA 30 ANYS.

TRACTATS AMB DOSI DE 35 – 45Gy.

1.490 CÀNCERS

625 CÀNCERS ESPERABLES

865 CÀNCERS EN EXCÉS



	HOMES	DONES
HODGKIN	18 %	26 %
POBLACIÓ GLOBAL	7 %	9 %

	20a	30a	40a	20a	30a	40a
HODGKIN	10.5 %	18 %	27 %	24.6 %	26 %	27 %
POBLACIÓ G	2.4 %	7 %	17.4 %	4.5 %	9 %	15.4 %

Table 3. Relative Risk of SC After HL

Cancer Site	No. of Second Cancers: 5-Year Survivors	10-Year Survivors	RR*	95% CI	Estimated No. of Excess SC
Solid cancers, all	1,490	1,001	—	—	850.4†
Female breast	277	226	6.1‡	4.7 to 7.6	174.8
Supra-and infradiaphragmatic, all	769	483	4.6	4.1 to 5.2	469.1†
Supradiphragmatic, all	414	239	6.0	5.2 to 6.9	298.5†
Buccal§	69	46	5.1	3.5 to 7.0	49.1
Esophagus	16	11	4.2	1.8 to 7.8	9.3
Lung	306	173	6.7	5.6 to 7.8	225.5
Pleura	6	6	19.5	7.3 to 40.3	5.4
Other supradiaphragmatic‖	17	11	3.0	1.3 to 5.7	9.1
Infradiaphragmatic, all	355	244	3.7	3.2 to 4.3	170.6†
Stomach	64	50	9.5	6.9 to 12.6	46.1
Colon	110	74	4.3	3.2 to 5.6	53.5
Rectum and anus	35	22	1.8	1.0 to 3.0	8.8
Pancreas	33	25	4.7	2.9 to 7.1	18.5
Urinary bladder	42	19	1.0¶	0.6 to 1.59	8.9#
Kidney	32	25	3.1	1.9 to 4.8	14.7
Other infradiaphragmatic**	39	29	4.6	2.9 to 6.8	20.1
Thyroid	40	32	3.1††	1.8 to 5.2	29.2
Other solid cancers	404	260	2.3	2.0 to 2.7	177.2†
Brain	33	19	1.8	1.1 to 2.7	15.6
Soft tissue and bone	49	33	11.7	8.2 to 16.1	44.3
Female genital	70	48	2.2	1.6 to 2.9	29.7
Prostate	104	54	1.0¶	0.8 to 1.3	11.5#
Melanoma	54	34	1.6	1.1 to 2.3	20.3
Primary site unspecified	70	56	10.6	7.8 to 13.9	51.8
All other specified sites‡‡	24	16	1.4¶	0.8 to 2.3	3.9

Abbreviations: SC, solid cancers; HL, Hodgkin's lymphoma; RR, relative risk

RR	NºExcés	%
19.5	5.4	0.6
11.7	44	5.1
10.6	52	5.9

	RR	NºExcés	% dels 2º CÀNCERS
PULMÓ	6.7	225/865	26%
MAMA	6.1	175/865 175/417 dones	20% 42% dones
COLON I RECTE	6.1	61/865	7%

Àrea Integral de Salut Barcelona Esquerra

MALALTIA CARDÍACA

blood

2011 117: 412-418
Prepublished online September 21, 2010;
doi:10.1182/blood-2010-06-291328

Clinically significant cardiac disease in patients with Hodgkin lymphoma treated with mediastinal irradiation

Shira L. Galper, James B. Yu, Peter M. Mauch, Jon F. Strasser, Barbara Silver, Ann LaCasce, Karen J. Marcus, Mary Ann Stevenson, Ming Hui Chen and Andrea K. Ng

1969 – 1998. 1279 pacients amb RT mediastínica. Dosis 35 – 45 Gy

Edat Mitja 25 anys.

Seguiment 20 anys

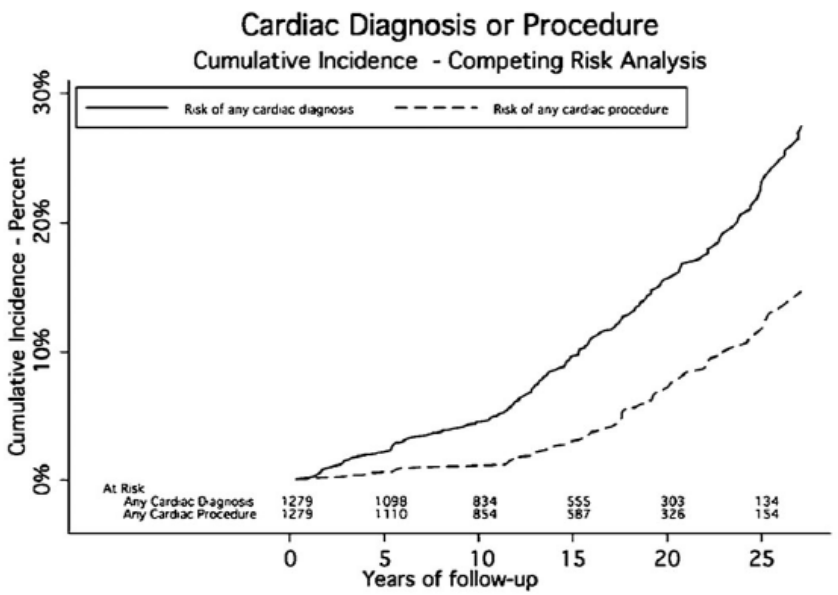


Figure 1. Cumulative incidence rates of any cardiac diagnosis or procedure.

15 anys	20 anys	30 anys
5 –10%	16%	34%

MALALTIA CORONÀRIA 40 – 50 % DELS EVENTS CARDÍACS. CARDIOMIOPATIA RESTRICTIVA. VALVULOPATIA…

MAJOR TOXICITAT AMB QUIMIOTERÀPIA.

MAJOR TOXICITAT CORONÀRIA AMB FACTORS DE RISC CONVENCIONALS.

MILLORAREM ?.

DISFUNCIÓ DE TIROIDES

The New England Journal of Medicine 1991
Vol. 325 No. 9 THYROID DISEASES AFTER TREATMENT OF HODGKIN'S DISEASE — HANCOCK ET AL.

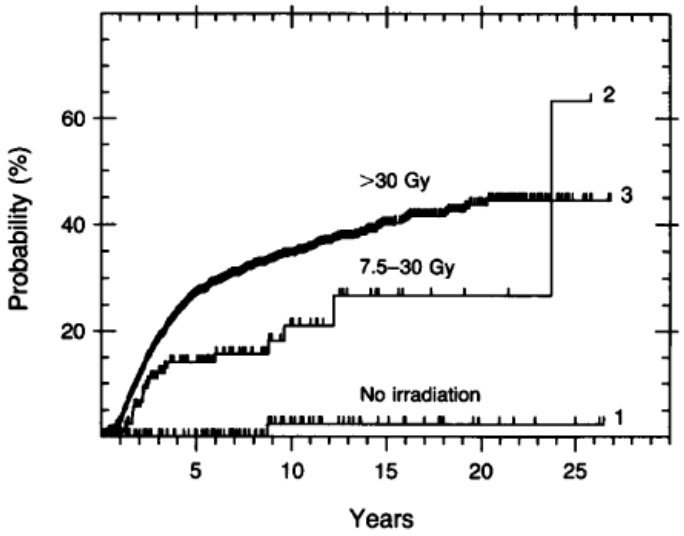
THYROID DISEASES AFTER TREATMENT OF HODGKIN'S DISEASE

STEVEN L. HANCOCK, M.D., RICHARD S. COX, PH.D., AND I. ROSS MCDOUGALL, M.B.

1961 – 1989. 1787 pacients amb RT en MANTLE. Dosis 35 – 45 Gy

Risc actuarial de Malaltia de Tiroides

20 anys	30 anys
16%	34%



Risc d'HIPOTIROIDISME 44% als 25 anys

U de Minnesota 60% als 11 anys

RR relatiu de càncer de Tiroides = 16

TOXICITAT PULMONAR

LA COMBINACIÓ DE RADIOTERÀPIA I QUIMIOTERÀPIA INCLOENT BLEOMICINA > TOXICITAT PULMONAR.

FUNCIÓ RESPIRATÒRIA ANORMAL EN 30% DELS SUPERVIVENTS.

PATRÓ RESTRICTIU AMB TOS SECA, DÍSPNEA, FEBRÍCULA I DOLOR PLEURÍTIC. ↓FEV1, FVC, DLCO.

Effect of ABVD Chemotherapy With and Without Mantle or Mediastinal Irradiation on Pulmonary Function and Symptoms in Early-Stage Hodgkin's Disease

By Arica Hirsch, Nicholas Vander Els, David J. Straus, Elizabeth G. Gomez, Denis Leung, Carol S. Portlock, and Joachim Yahalom

Conclusion: **ABVD chemotherapy induced acute pulmonary toxicity that required bleomycin dose modification in a substantial number of patients. The addition of RT resulted in a further decrease in FVC; however, this did not significantly affect the functional status of patients.**

J Clin Oncol 14:1297-1305. © 1996 by American Society of Clinical Oncology.

Anticancer Res. 1997 Nov-Dec;17(6D):4739-42.

Late pulmonary toxicity after treatment for Hodgkin's disease.

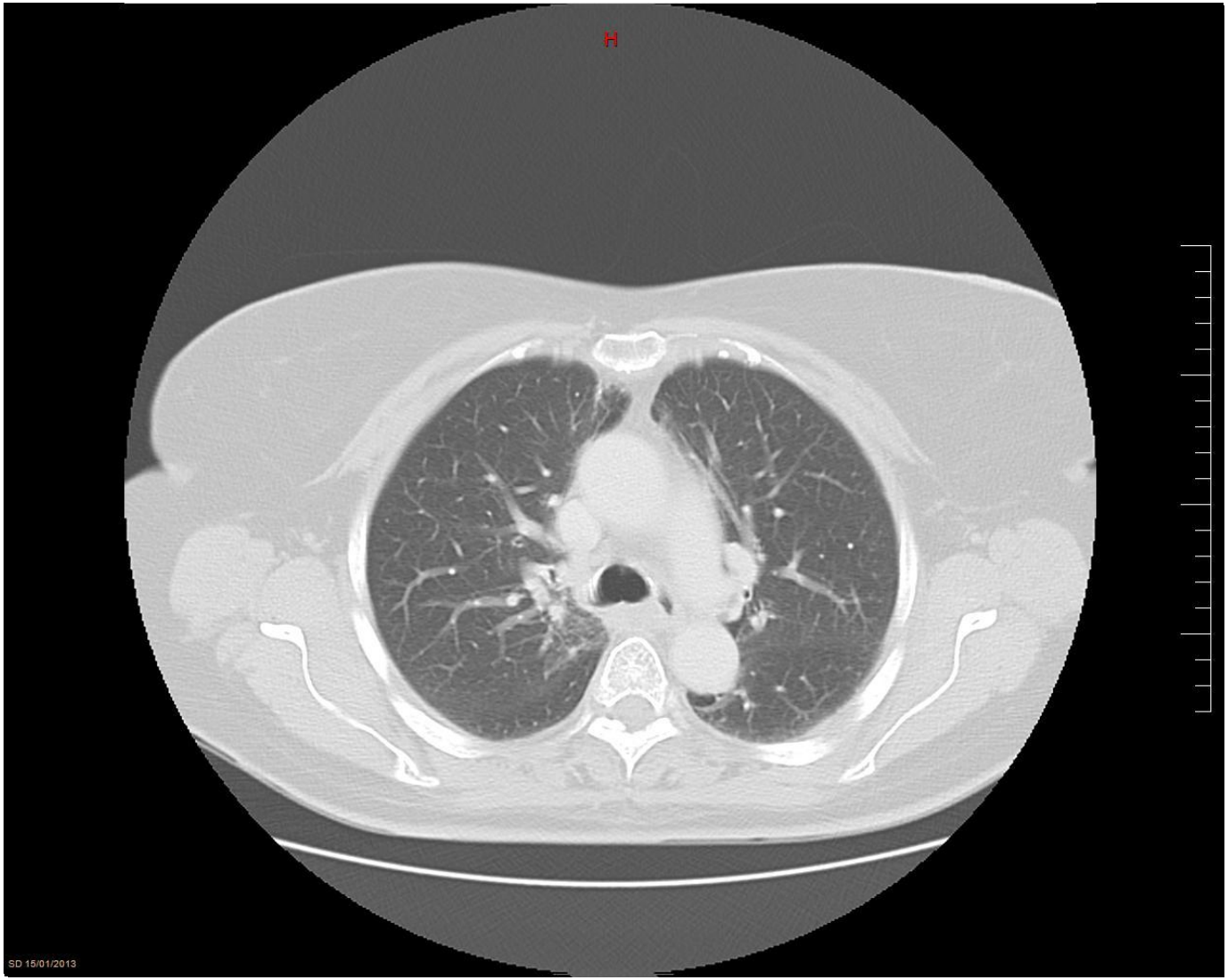
Villani F[1], De Maria P, Bonfante V, Viviani S, Laffranchi A, Dell'oca I, Dirusso A, Zanini M.

Author information

Abstract

The combination of mediastinal radiotherapy (RT) with chemotherapy (CT) including bleomycin is associated with an increased risk of pulmonary toxicity. The aim of the present investigation was to evaluate late pulmonary effects of RT plus CT consisting of the ABVD regimen in patients suffering from early stage Hodgkin's disease. For this purpose pulmonary function was serially evaluated before, at the end and at least 1 year after therapy in 32 patients (median age 28 years) with Hodgkin's disease stages IA,B-IIA. Treatment consisted of four cycles of ABVD chemotherapy followed by mediastinal irradiation at the median dose of 36 Gy (range 30.6-43.2). At the end of treatment, resting mean pulmonary function tests showed a significant decline of forced expiratory volume in 1 second (FEV1), forced expiratory flow at 25-75%, (FEF25-75%), total lung capacity (TLC), vital capacity (VC) and carbon monoxide diffusing capacity (DLCO). The decline of TLC, VC and DLCO, indicative of a pulmonary defect of restrictive type, persisted 1 year from the end of therapy. Only seven patients developed symptoms of cough and mild shortness of breath with effort. These data confirm that RT combined with short term ABVD result in pulmonary dysfunction that does not seem to have clinical significance.

TOXICITAT PULMONAR



FOLLOW-UP AFTER COMPLETION OF TREATMENT AND MONITORING FOR LATE EFFECTS

- It is recommended that the patient be provided with a treatment summary at the completion of his/her therapy.
- Follow-up with an oncologist is recommended, especially during the first 5-y interval to detect recurrence, and then annually due to the risk of late complications including second cancers and cardiovascular disease.[dd,ee] Late relapse or transformation to large cell lymphoma may occur in LPHL.
- The frequency and types of tests may vary depending on clinical circumstances: age and stage at diagnosis, social habits, treatment modality, etc. There are few data to support specific recommendations; these represent the range of practice at NCCN Member Institutions.

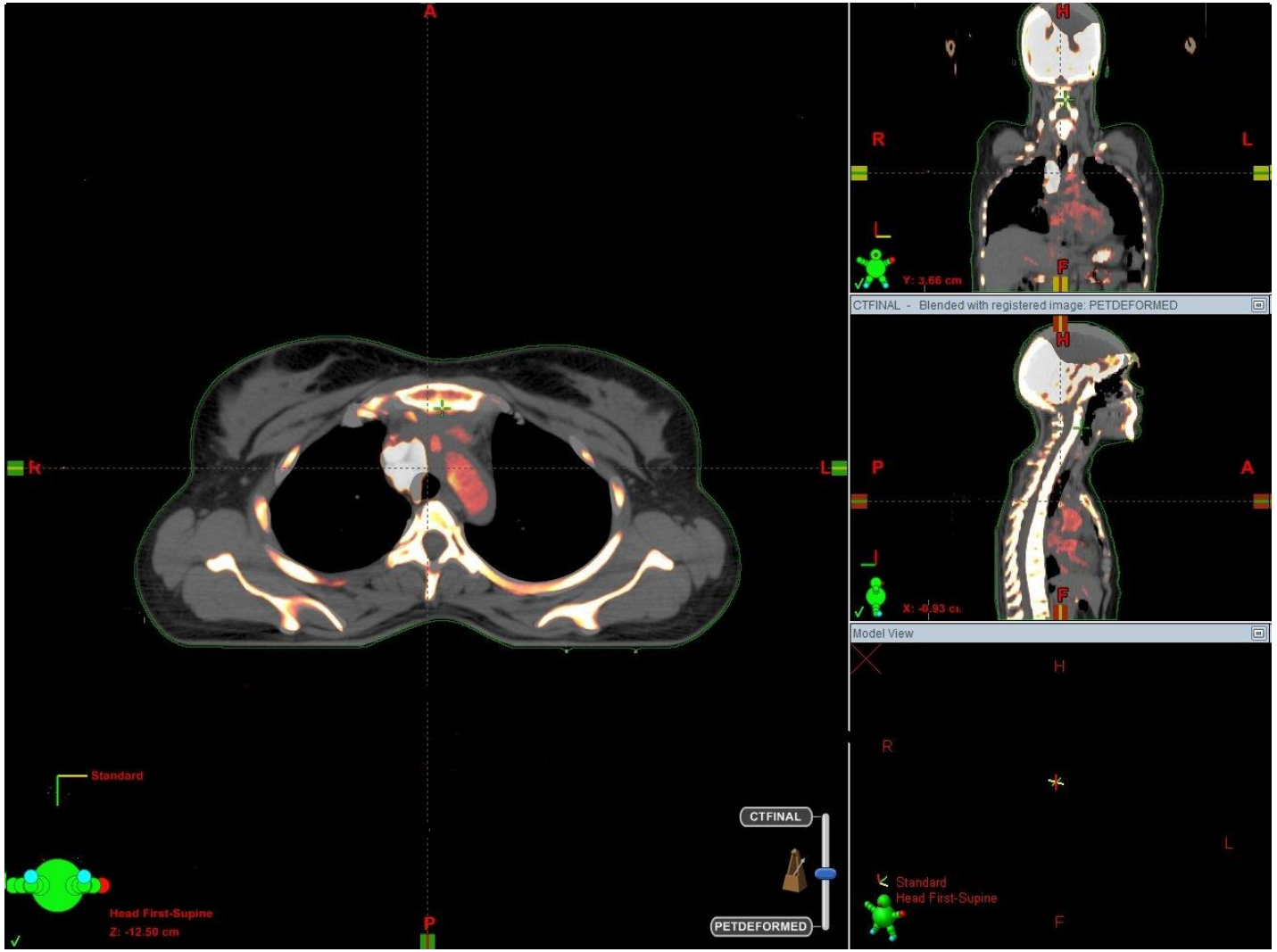
Follow-up After Completion of Treatment up to 5 Years

- Interim H&P:
  Every 2-4 mo for 1-2 y, then every 3-6 mo for next 3-5 y
  - Annual influenza vaccine
- Laboratory studies:
  - CBC, platelets, ESR (if elevated at time of initial diagnosis), chemistry profile every 2-4 mo for 1-2 y, then every 3-6 mo for next 3-5 y
  - Thyroid-stimulating hormone (TSH) at least annually if RT to neck
- Chest x-ray or CT every 6-12 mo during first 2-3 y, then chest x-ray optional
- Abdominal/pelvic CT every 6-12 mo for first 2-3 y
- Counseling:
  Reproduction, health habits, psychosocial, cardiovascular, breast self-exam, skin cancer risk, end-of-treatment discussion.
- Surveillance PET should not be done routinely due to risk for false positives. Management decisions should not be based on PET scan alone; clinical or pathologic correlation is needed.

Suspected Relapse CHL (HODG-17) or LPHL (HODG-18)

Monitoring for Late Effects After 5 Years[dd,ee]

- Interim H&P: Annually
  - Annual blood pressure, aggressive management of cardiovascular risk factors
  - Pneumococcal, meningococcal, and H-flu revaccination after 5-7 y, if patient treated with splenic RT or previous splenectomy
  - Annual influenza vaccine
- Consider baseline stress test/echocardiogram at 10 y, especially if chest irradiation
- Consider carotid ultrasound, especially if neck irradiation
- Laboratory studies:
  - CBC, platelets, chemistry profile annually
  - TSH at least annually if RT to neck
  - Annual lipids
- Consider chest imaging for patients at increased risk for lung cancer[ff]
- Annual breast screening:
  Initiate 8-10 y post-therapy, or at age 40, whichever comes first, if chest or axillary radiation. The NCCN Hodgkin Lymphoma Guidelines Panel recommends breast MRI in addition to mammography for women who received irradiation to the chest between ages 10 and 30 y, which is consistent with the American Cancer Society Guidelines.
- Counseling:
  Reproduction, health habits, psychosocial, cardiovascular, breast self-exam, skin cancer risk.
- Cardiovascular symptoms may emerge at a young age.
- Treatment summary and consideration of transfer to PCP.



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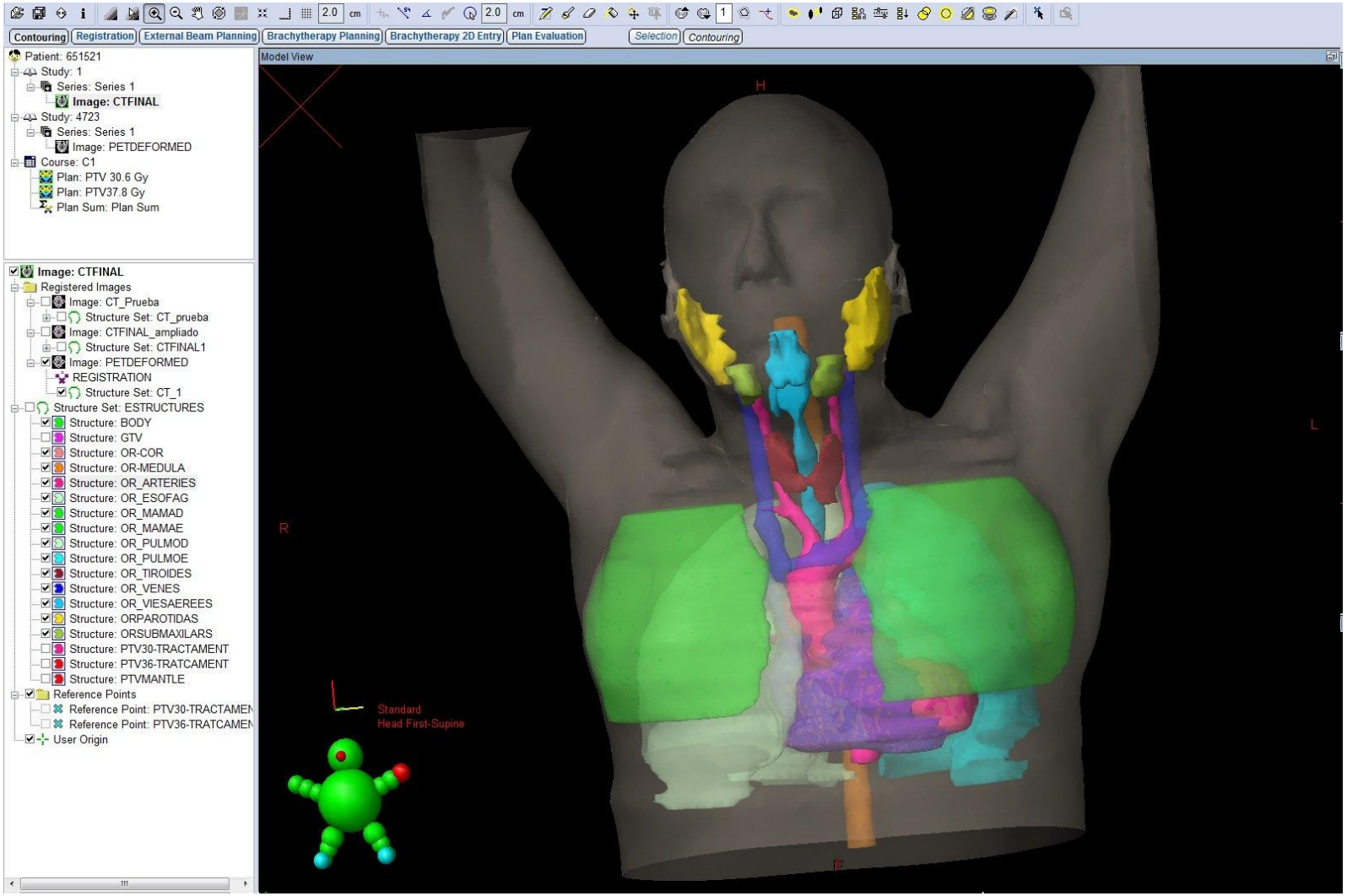

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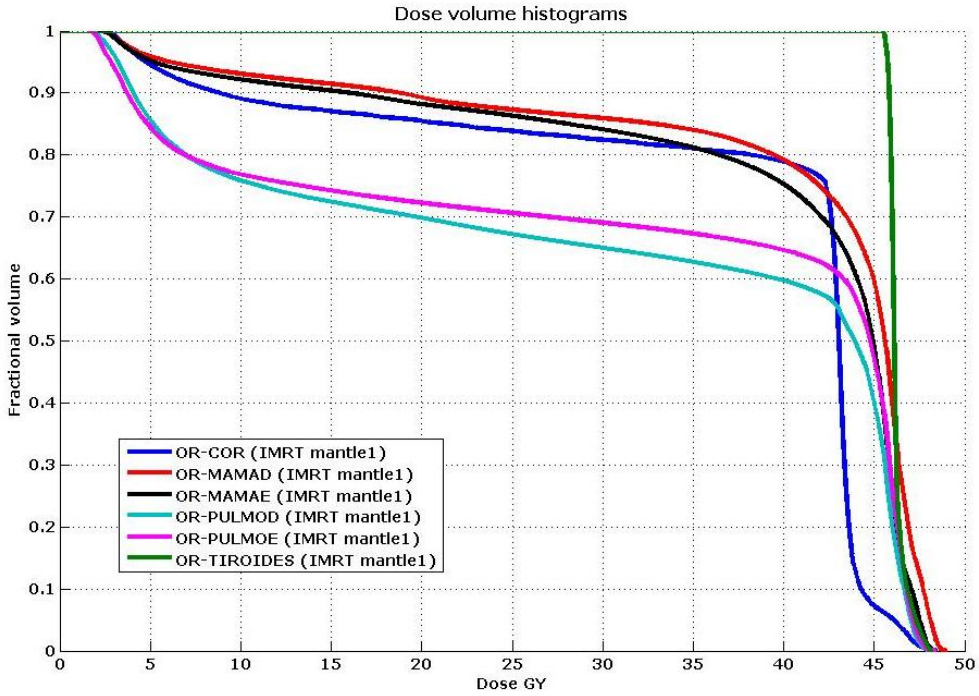
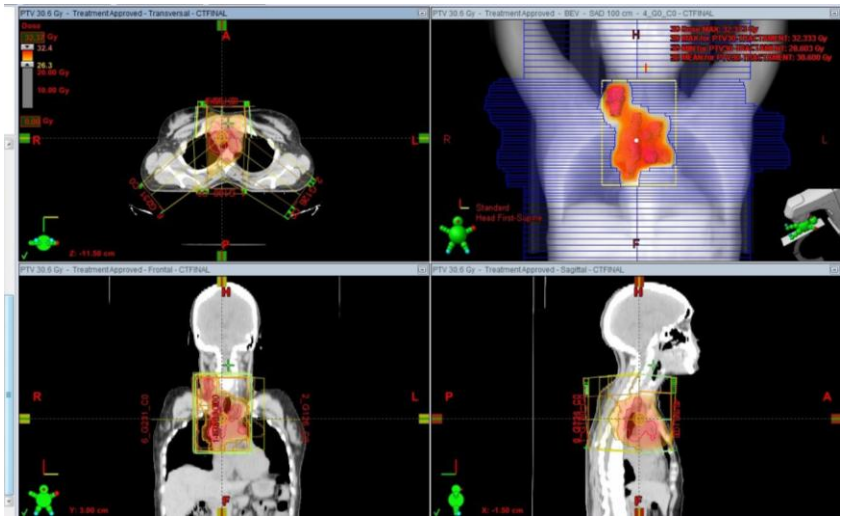
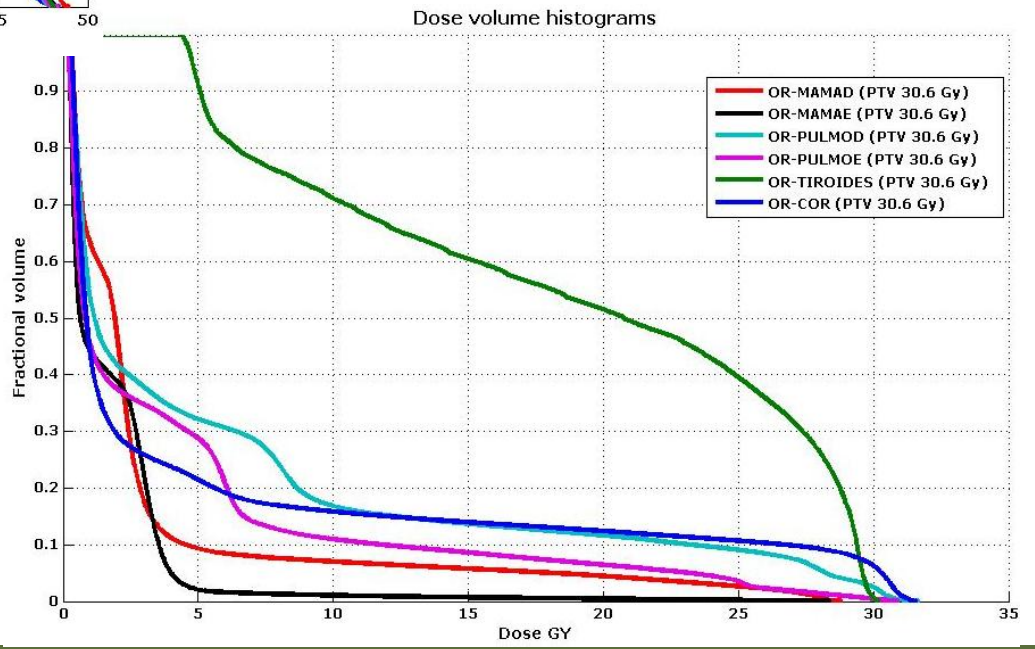
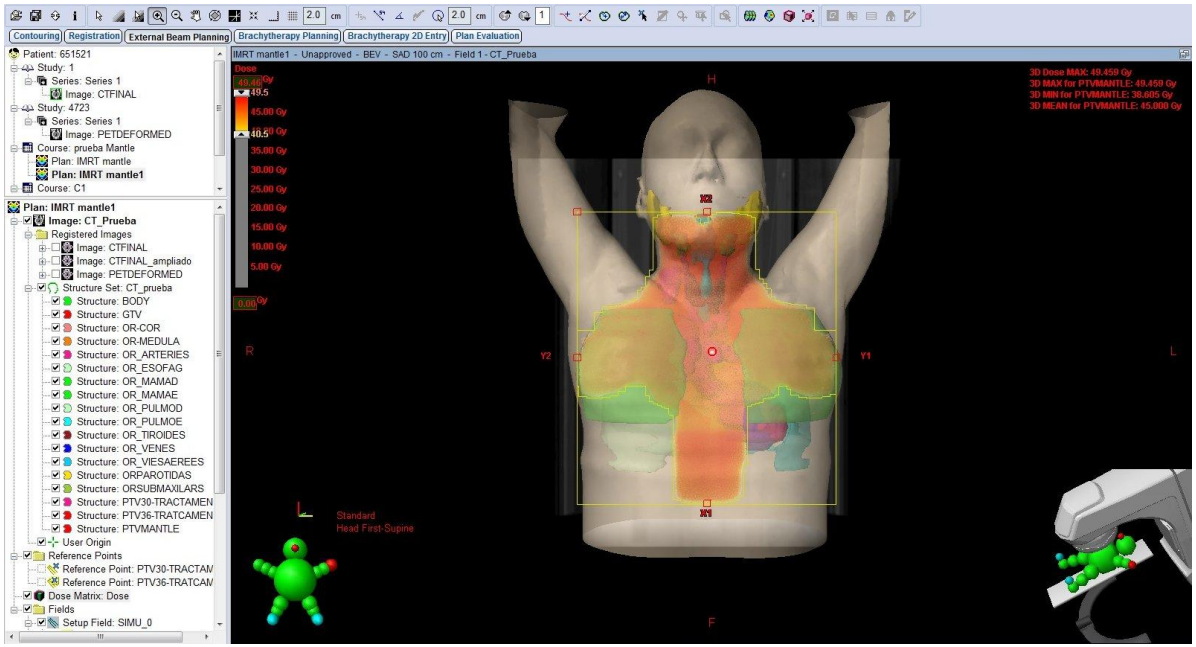
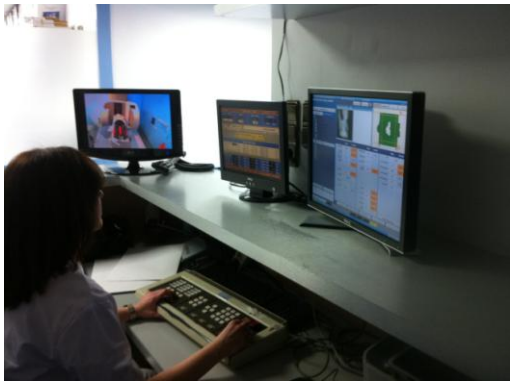
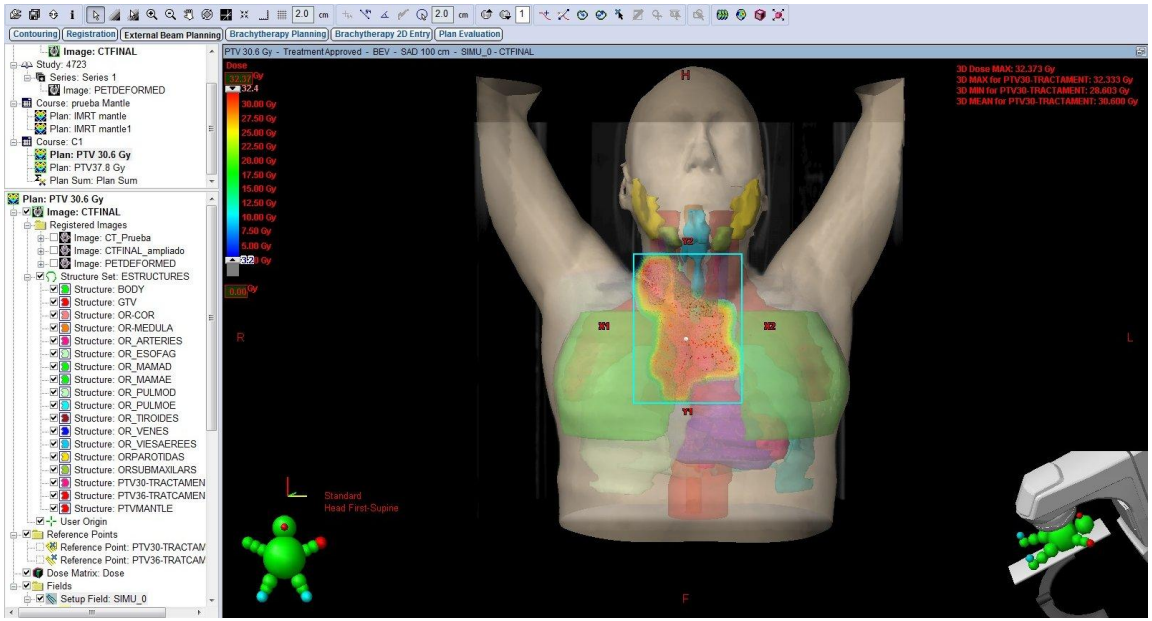

Dose volume histograms
Fractional volume
Dose GY
OR-COR (IMRT mantle1)
OR-MAMAD (IMRT mantle1)
OR-MAMAE (IMRT mantle1)
OR-PULMOD (IMRT mantle1)
OR-PULMOE (IMRT mantle1)
OR-TIROIDES (IMRT mantle1)




Dose volume histograms
Fractional volume
Dose GY
OR-MAMAD (PTV 30.6 Gy)
OR-MAMAE (PTV 30.6 Gy)
OR-PULMOD (PTV 30.6 Gy)
OR-PULMOE (PTV 30.6 Gy)
OR-TIROIDES (PTV 30.6 Gy)
OR-COR (PTV 30.6 Gy)







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