RADIOTERAPIA REVOLUCIÓN EN LA MEDICINA

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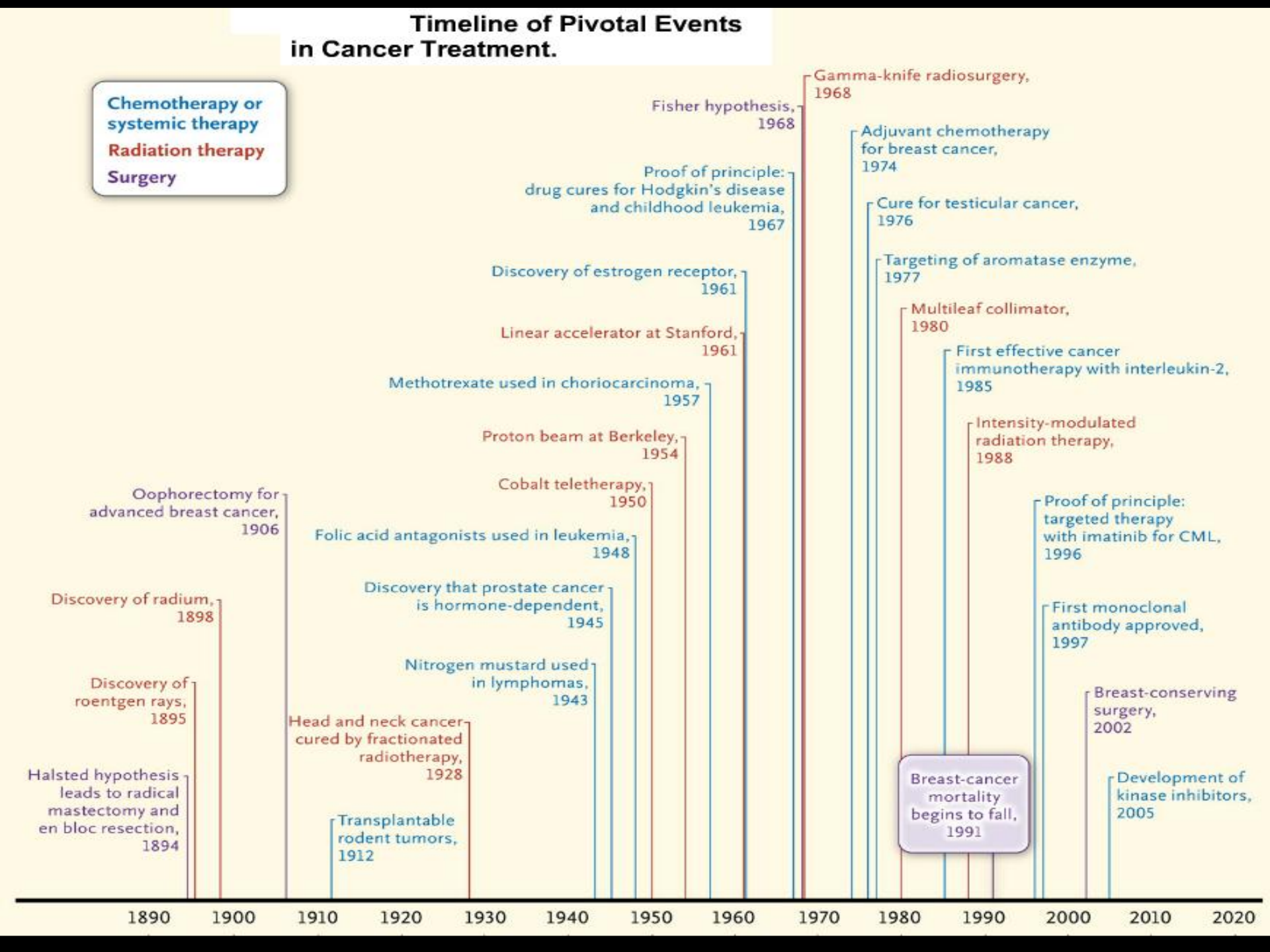
TECNOLOGÍA EN LA MEDICINA

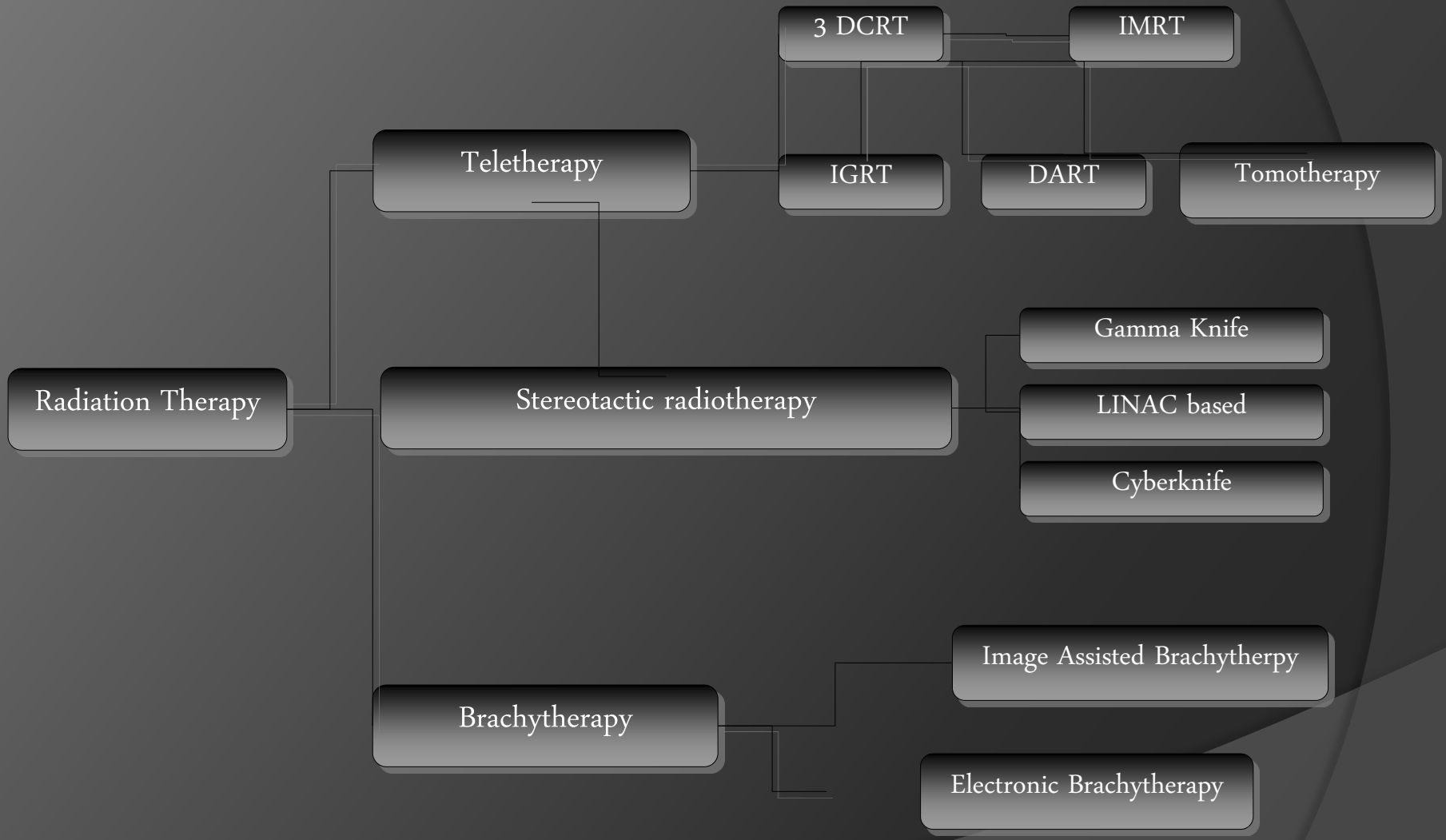
- 1895 W. C. Roenteng descubre los rayos X.
- 1921 por primera vez se utiliza un microscopio en una operación; actualmente en vez de microscopios, se utiliza la técnica “endoscopia” para realizar cualquier intervención quirúrgica demasiado pequeña para la vista humana.
- 1942 se utiliza por primera vez un riñón artificial para la diálisis; este sistema de órganos artificiales se ha desarrollado significativamente por todo el mundo.
- 1952 P.M. Zoll implanta el primer marcapasos; son dispositivos eléctricos que hacen latir el corazón descargando impulsos eléctricos, que reemplazan el propio sistema de control del corazón.
- 1953 se obtiene el modelo de la doble hélice del ADN; se puede señalar que este descubrimiento revolucionó tanto la medicina como nuestra manera de pensar. En el año de 1991 se inició un programa, Análisis del Genoma Humano, que tiene como principal objetivo descifrar el código genético humano. Hasta la fecha se han identificado cerca de 18,000 genes. En un futuro, gracias a las nuevas computadoras, cada vez más especializadas, se identificará un gen cada hora.
- 1967 primer trasplante de corazón entre humanos. Hoy en día, estos trasplantes, gracias a la aplicación de la tecnología, es una operación relativamente sencilla.
- 1980 Scanner TAC (Tomografía Axial Computarizada) :No hay duda que las técnicas desarrolladas alrededor de la TAC han revolucionado la forma de diagnóstico de muchas enfermedades y sobre todo de lesiones en tejidos blandos. No se podría imaginar tener en la actualidad un hospital sin éste tipo de equipos

Timeline of Pivotal Events in Cancer Treatment.

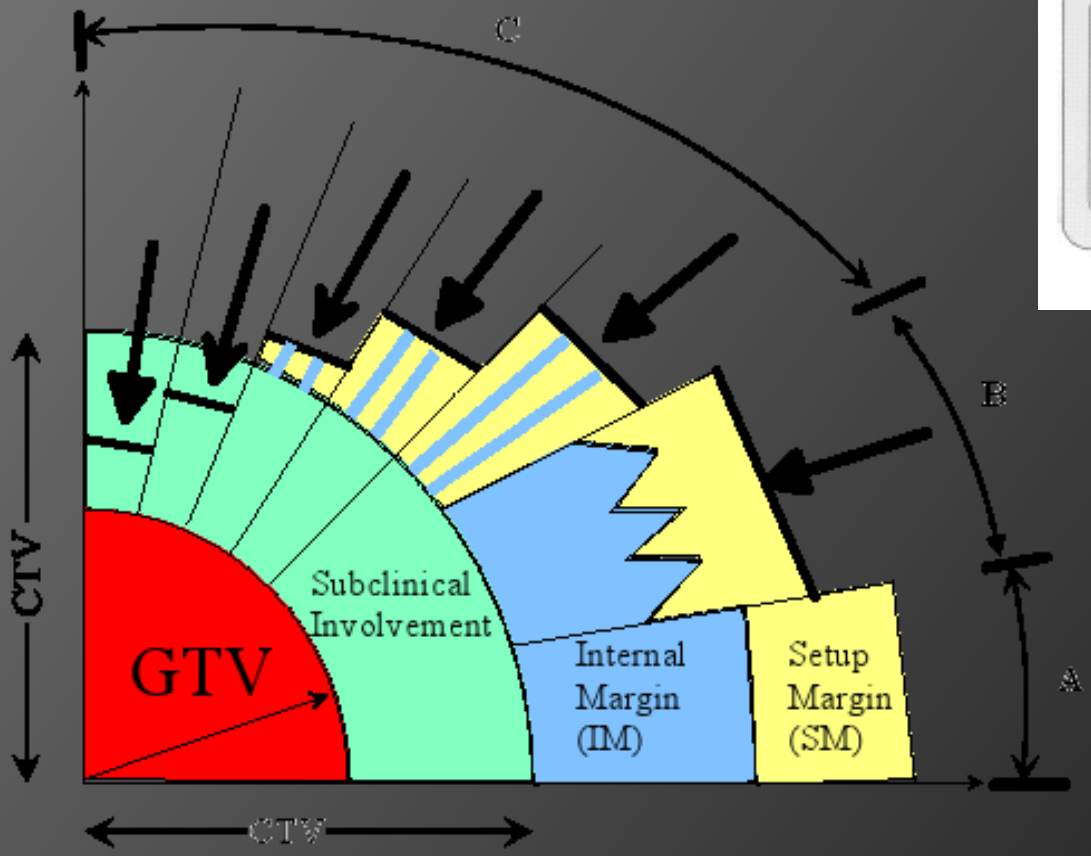


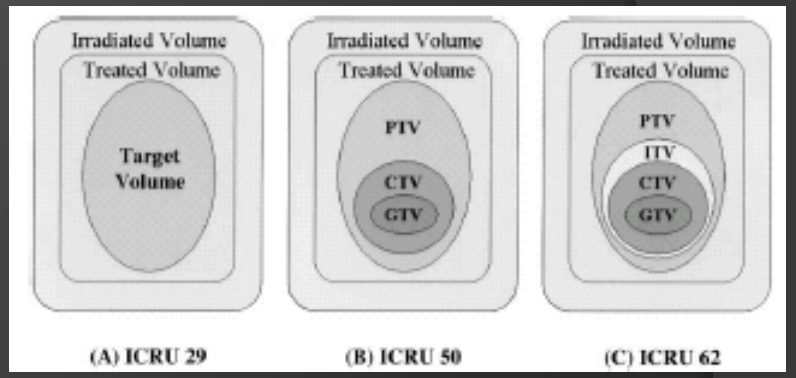
HISTORIA DE LA RADIOTERAPIA

- 1895 Descubrimiento de los rayos X
- 1896 Descubrimiento de la Radioactividad
- 1898 Descubrimiento del Radium
- 1920's mejoras en los tubos de RX (150-300Kv)
- 1950's Cobaltos (1Mv or million volt)
- 1960's Acelerador Lineal (4 - 25 million)
- 1970's computadoras y TAC
- 1980's Radioterapia 3D
- 1990's Radioterapia conformada 3D
- 2002 IMRT
- 2002+ IGRT

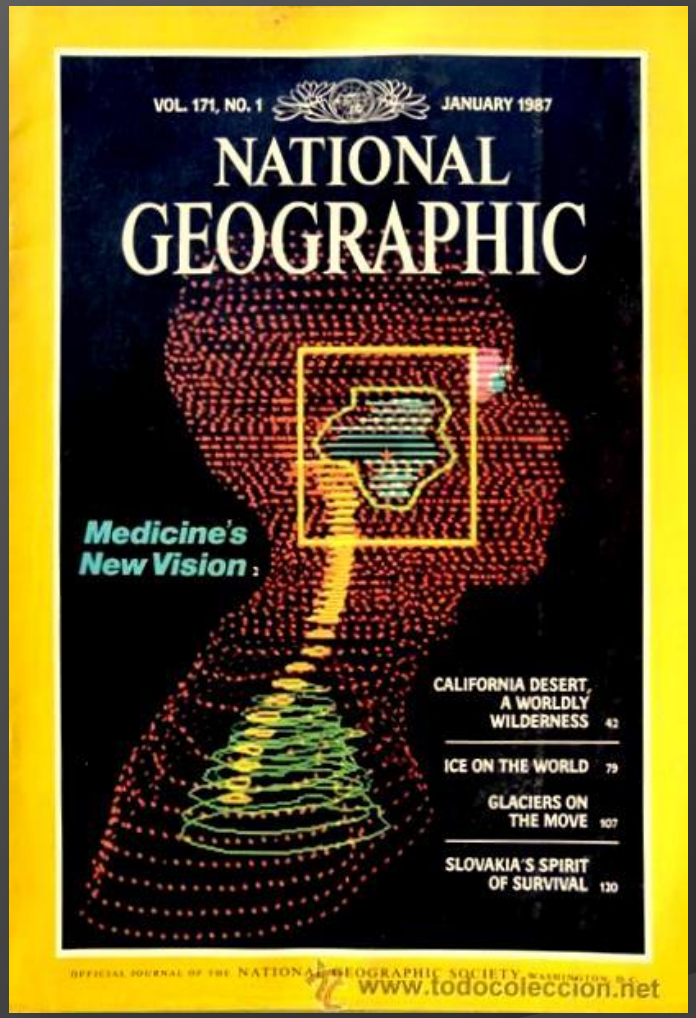

Radiation Therapy
Teletherapy
3 DCRT
IMRT
IGRT
DART
Tomotherapy
Stereotactic radiotherapy
Gamma Knife
LINAC based
Cyberknife
Brachytherapy
Image Assisted Brachytherpy
Electronic Brachytherapy


Use alternative radiation modalities
Electrons
Protons
Neutrons
π- Mesons
Heavy Charged Nuclei
Antiprotons

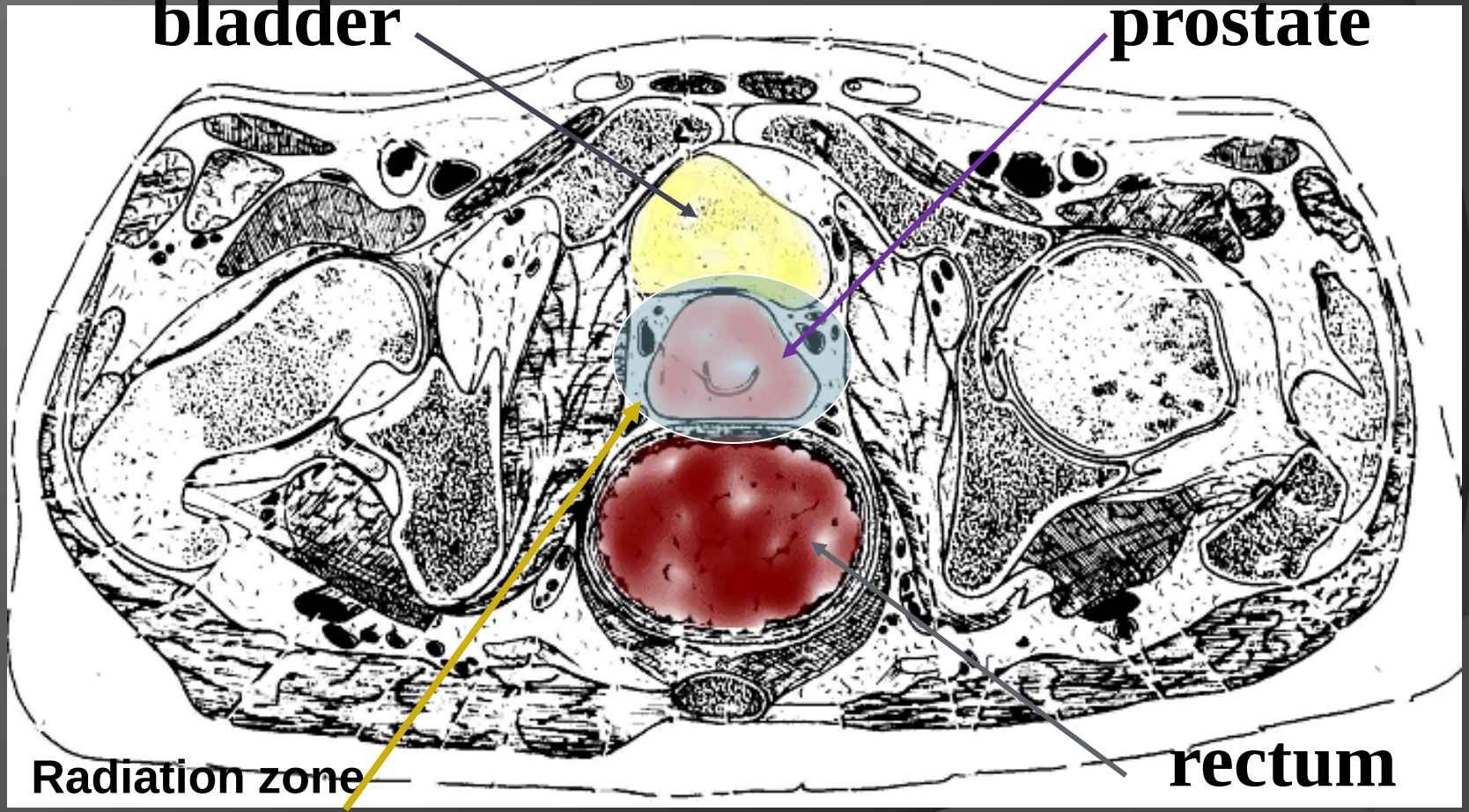

C
B
A
CTV
GTV
Subclinical Involvement
Internal Margin (IM)
Setup Margin (SM)
CTV

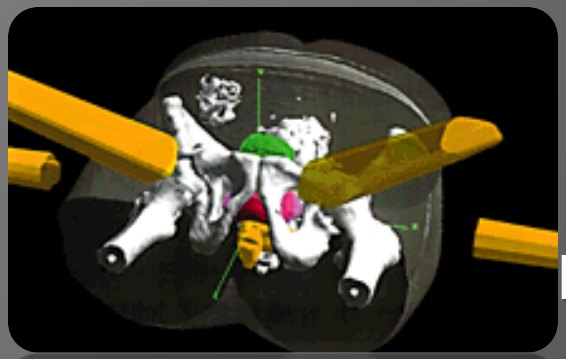

Irradiated Volume
Treated Volume
Target Volume
(A) ICRU 29
Irradiated Volume
Treated Volume
PTV
CTV
GTV
(B) ICRU 50
Irradiated Volume
Treated Volume
PTV
ITV
CTV
GTV
(C) ICRU 62

NUEVA VISION EN MEDICINA

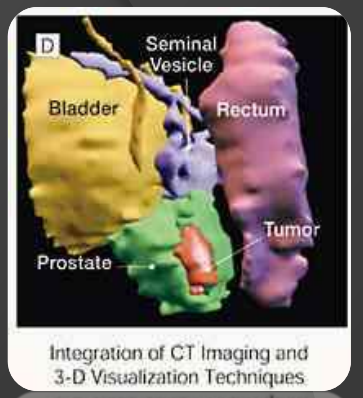


OBJETIVO = OCUPAR EL VOLUMEN BLANCON CON PEQUEÑOS MARGENES





Radioterapia conformada en 3D



Estudio randomizado en el MD Anderson

conventional	53%
conformal	**72%**

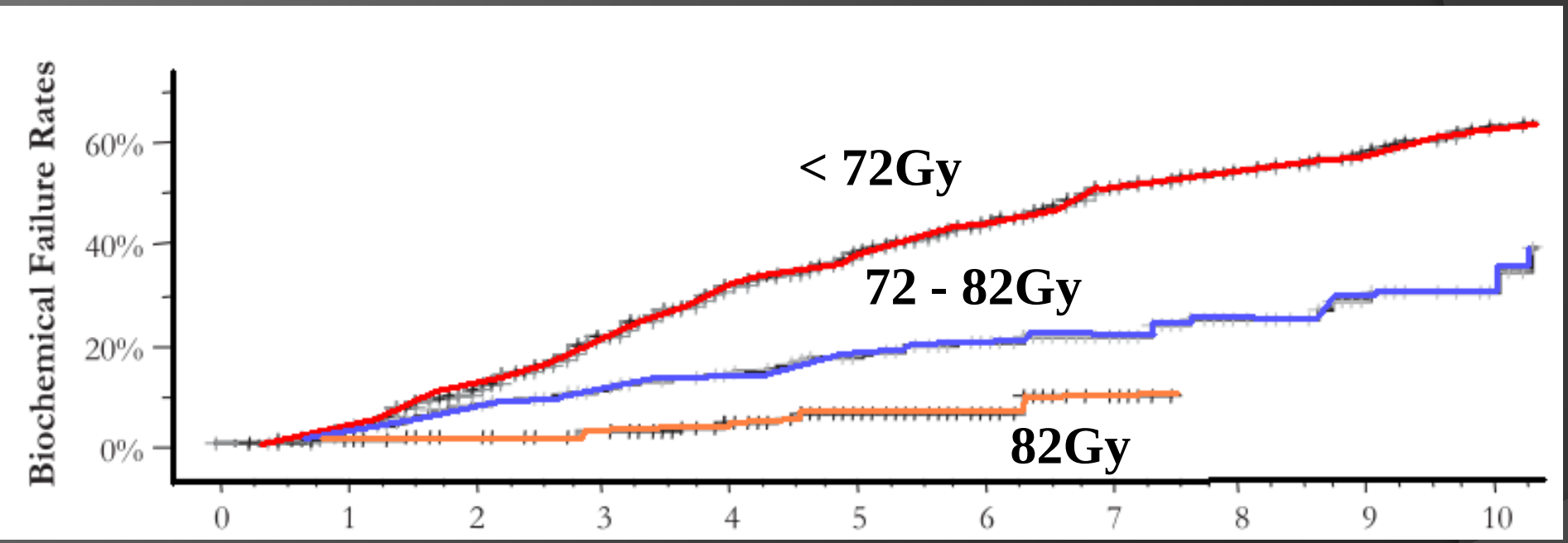
Pollack IRJOBP 1996;34:555

FDA Approval 4.29.10

median OS of 25.8 months compared to 21.7 months for patients who received the control treatment There was no difference in time-to-progression.

The total cost for three courses of treatment with Sipuleucel-T is $93,297.60

Recurrencia en Cáncer de Próstata y dosis de radiación

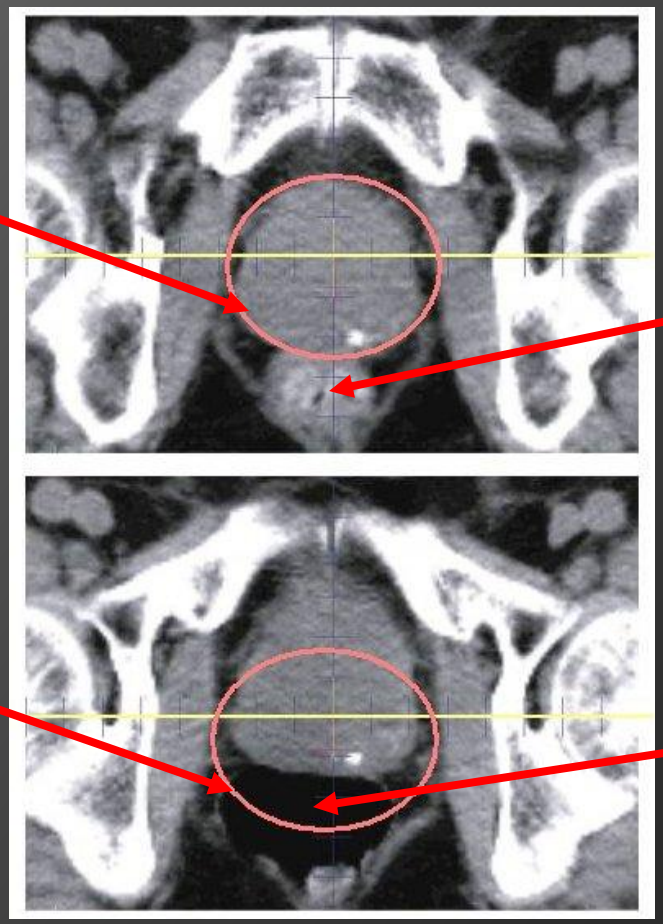


años

Kupelian. IJROBP 2008:71:16

Existe movimiento significativo de la próstata por el gas rectal

Planned target



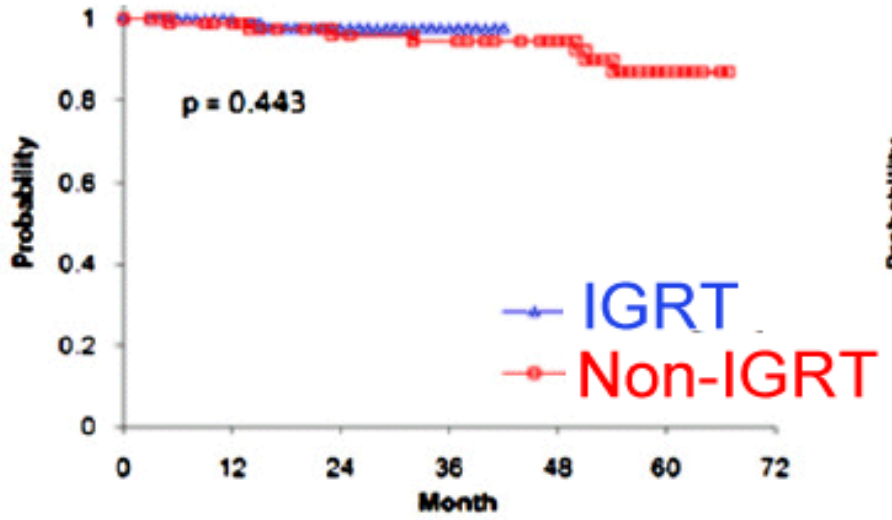
No Rectal gas

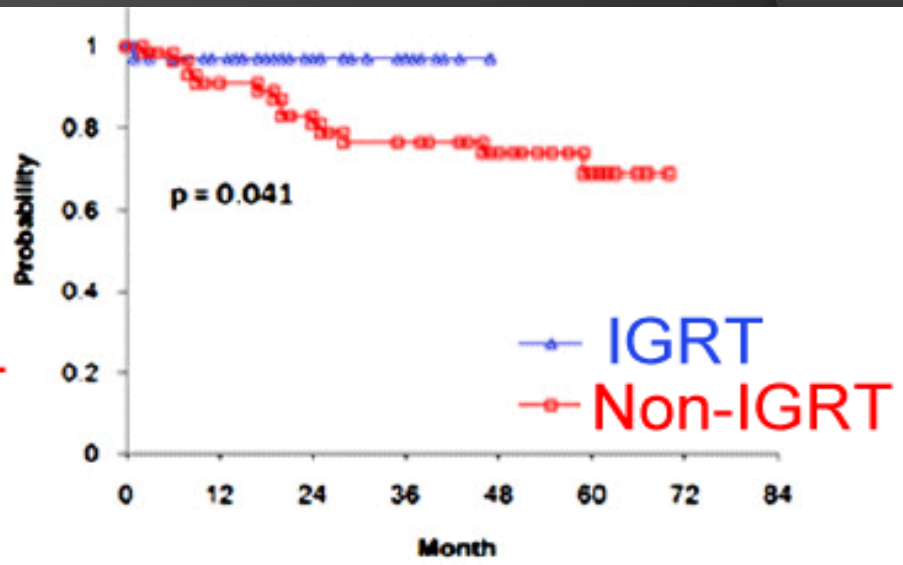
Planned target, missed badly if rectal gas pushes the prostate forward

Rectal gas

IGRT comparado a IMRT en cáncer de próstata

riesgo intermedio **alto riesgo**





Comparison of prostate specific antigen relapse-free survival outcomes between patients treated with image-guided radiotherapy (IGRT) to 86.4 Gy and those treated with intensity-modulated radiotherapy to the same dose level.

Zelefsky et al. International Journal of Radiation Oncology • Biology • Physics

Bajo riesgo de efectos secundarios con IGRT comparado a IMRT

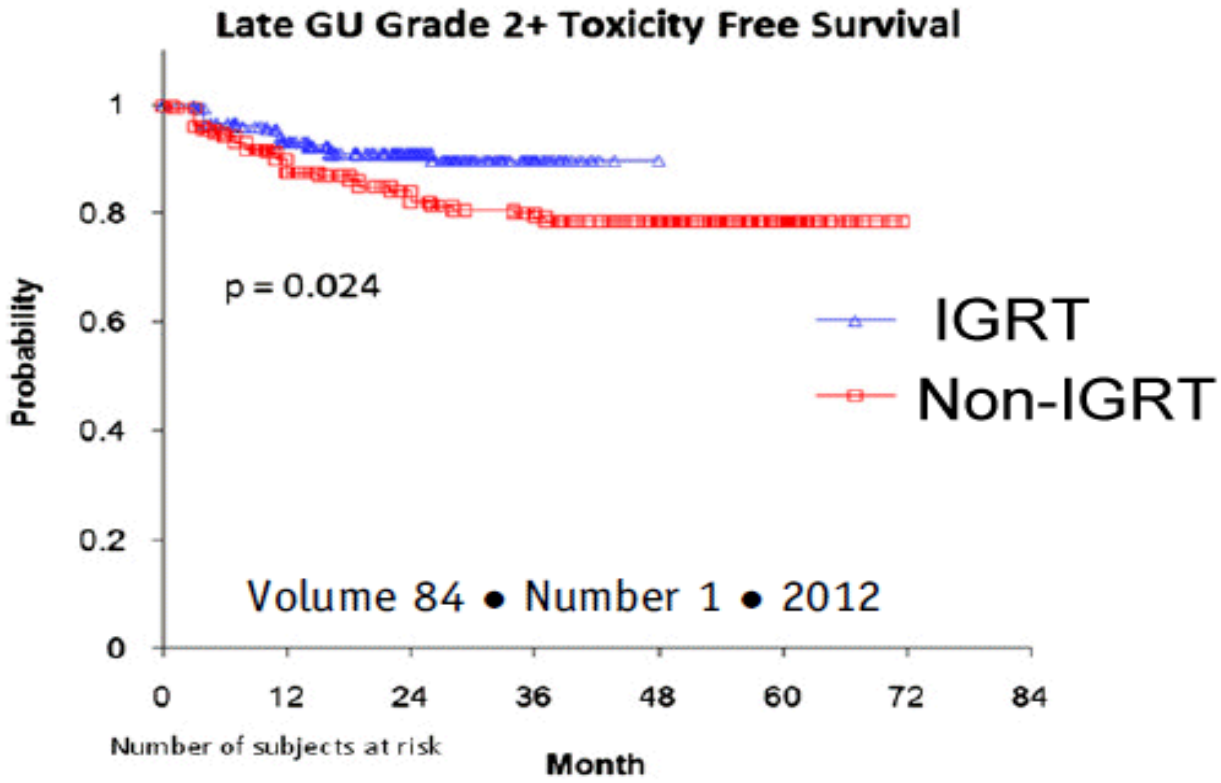
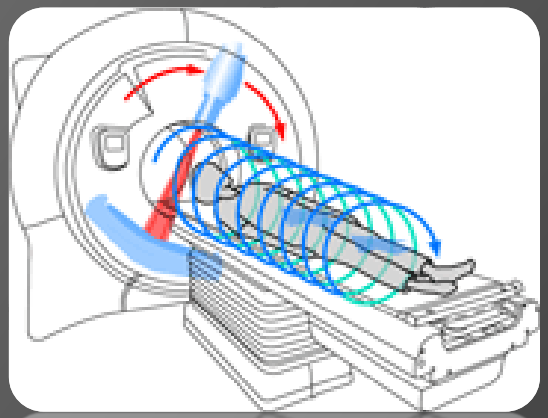
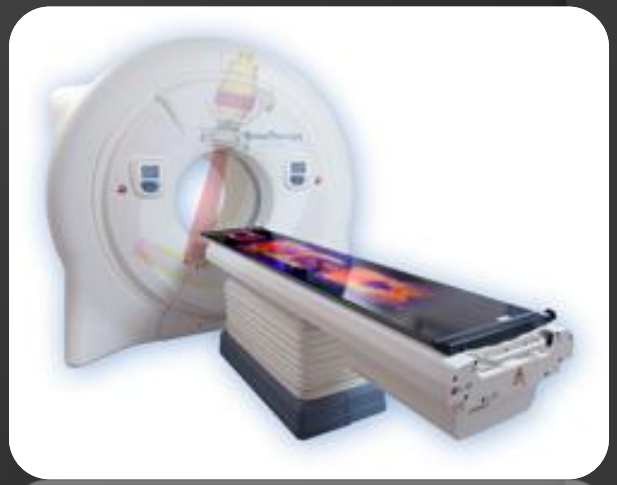


Fig. 1. Comparison of actuarial likelihood of grade 2 or higher late urinary toxicity for patients treated with image-guided radiotherapy (IGRT) to 86.4 Gy vs. intensity-modulated radiotherapy.

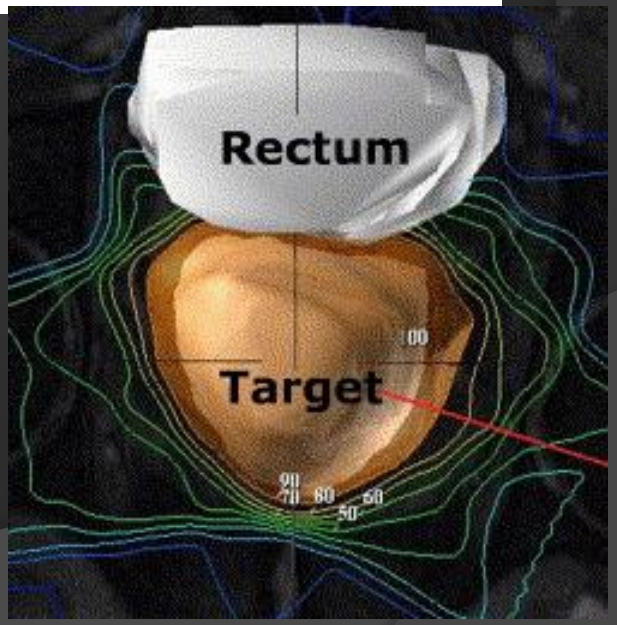
TomoTherapy®



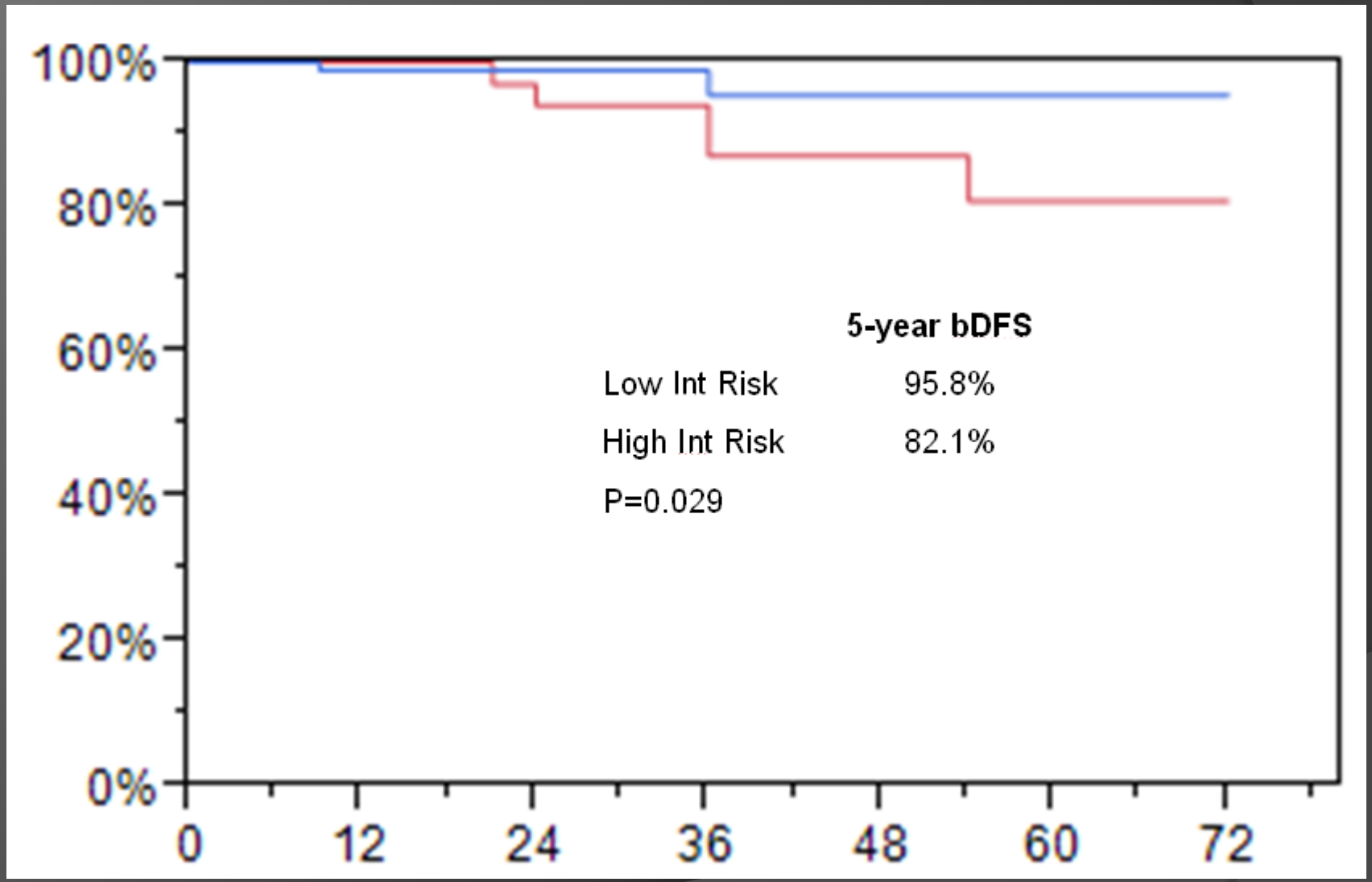


Combine a CT scan and linear accelerator to ultimate in targeting (IGRT) and ultimate in delivery (dynamic, helical IMRT) ability to daily adjust the beam (ART or adaptive radiotherapy)

Cyberknife



TASAS DE CURACION EN CANCER DE PROSTATA CON CYBERKNIFE

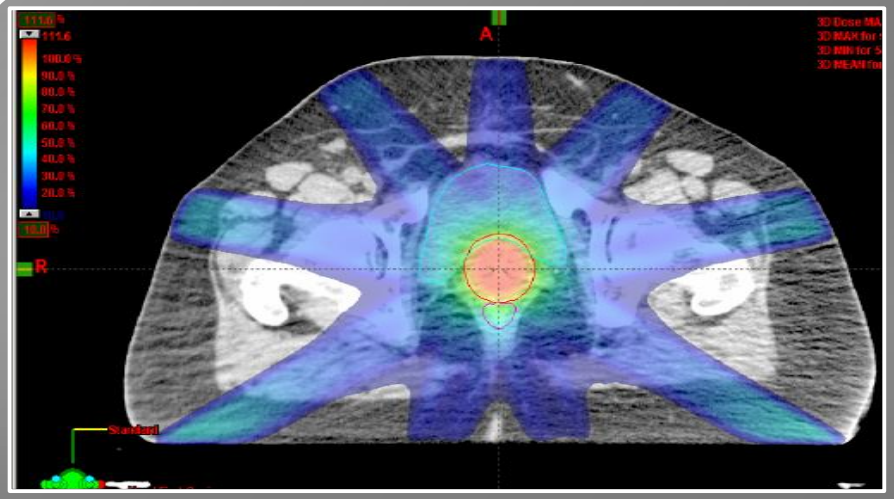


N = 515, Alan Katz in New York

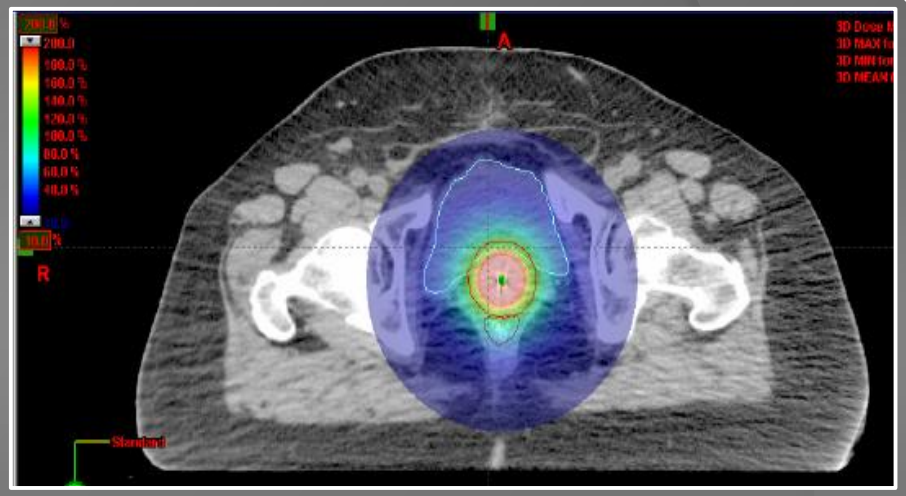
SBRT EN CÁNCER DE PROSTATA / Naples-Tampa

- Feb 2005 – Apr 2008 (Naples, FL)
  - 164 monotherapy, 35 Gy
  - 168 monotherapy, 36.25 Gy
  - 59 EBRT + CK boost
- Jul 2008 – Dec 2011 (Tampa, FL)
  - 121 monotherapy, 36.25 Gy
  - 10 monotherapy, 38 GY
  - 12 EBRT + CK boost

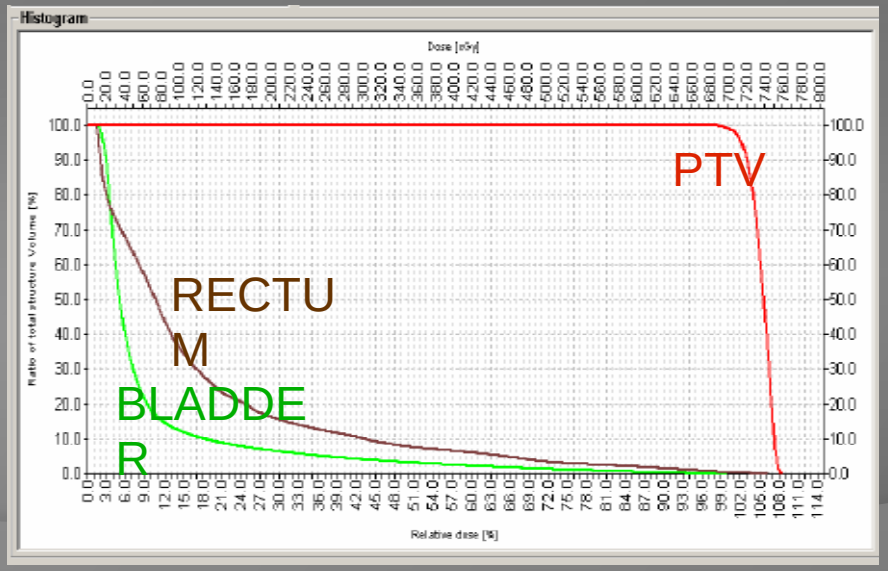
IMRT Vs BRAQUITERAPIA

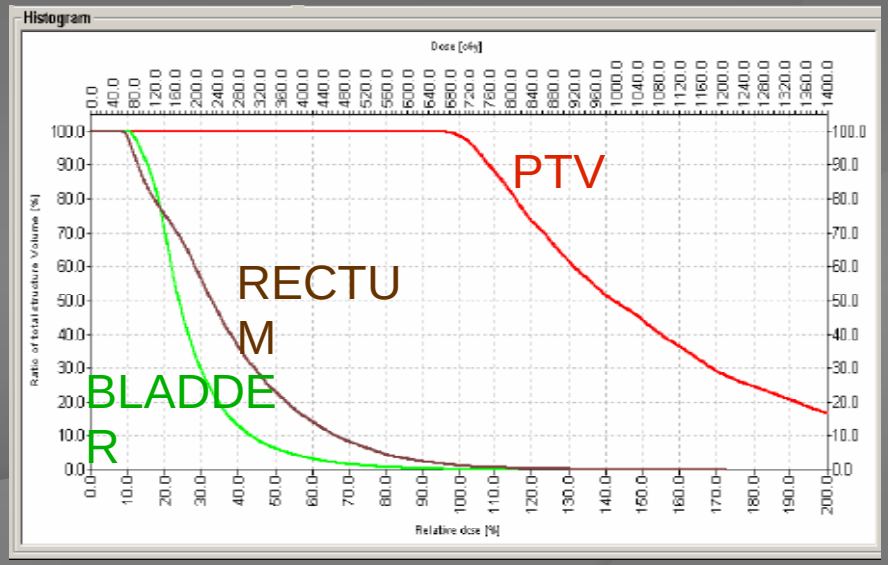


I M R T

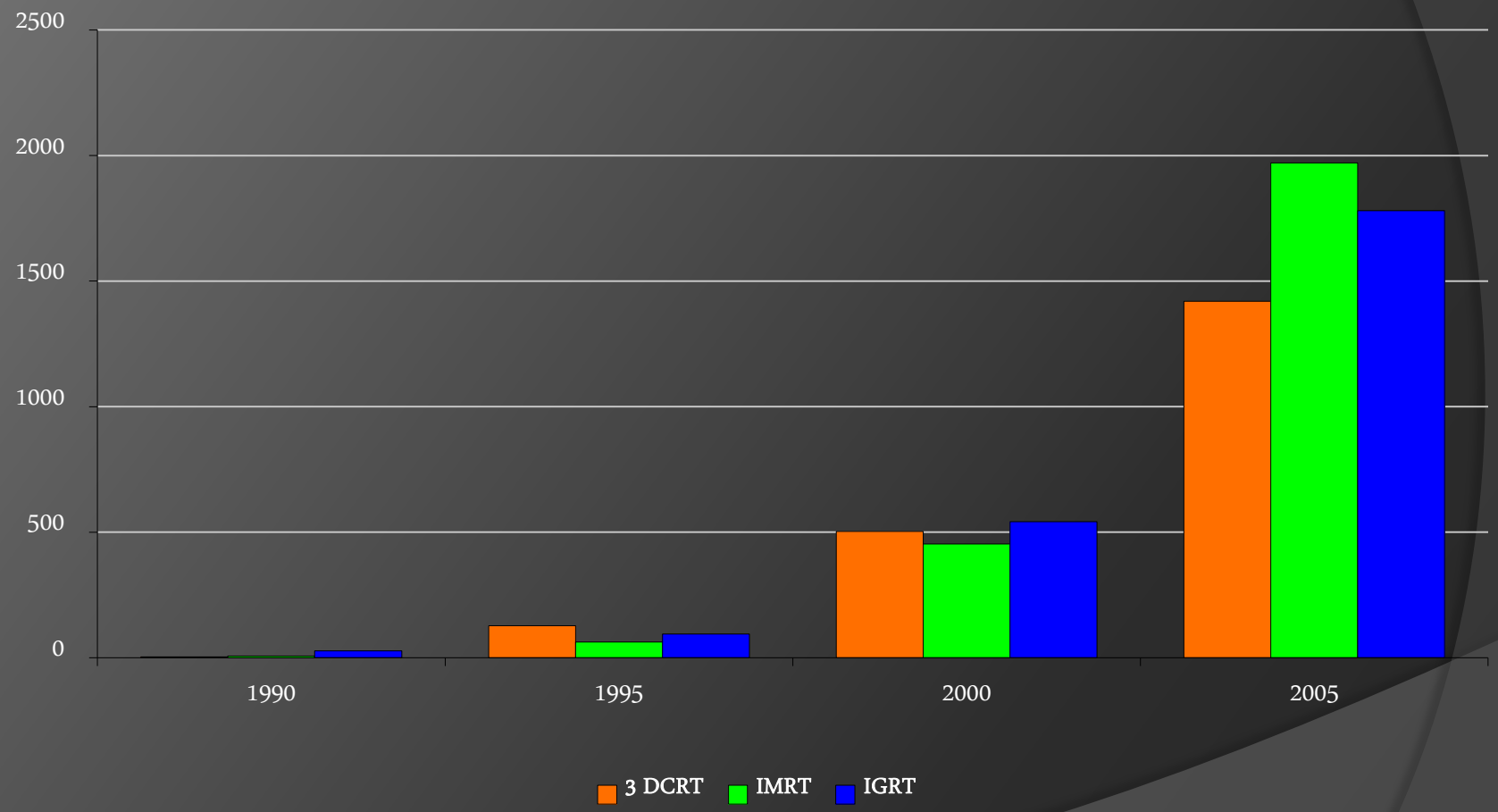


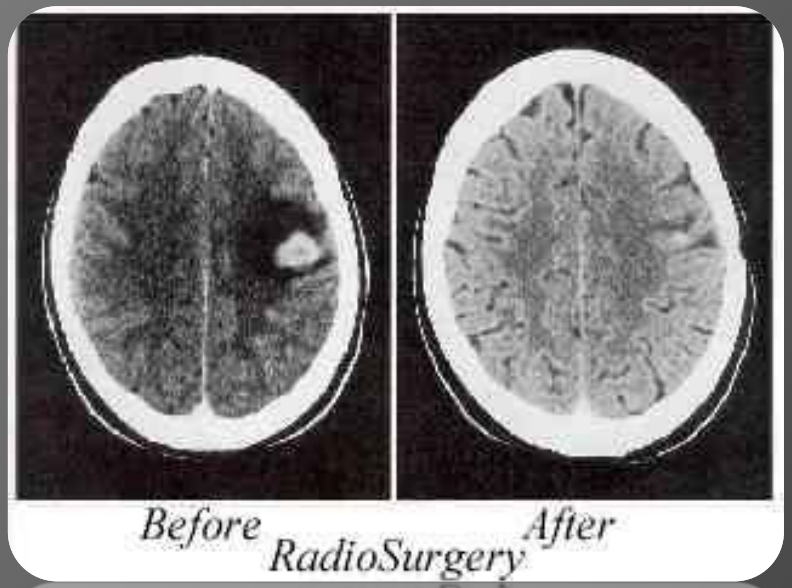
BRACHYTHERAPY





Número de publicaciones en Google Scholar





METASTASIS CEREBRAL

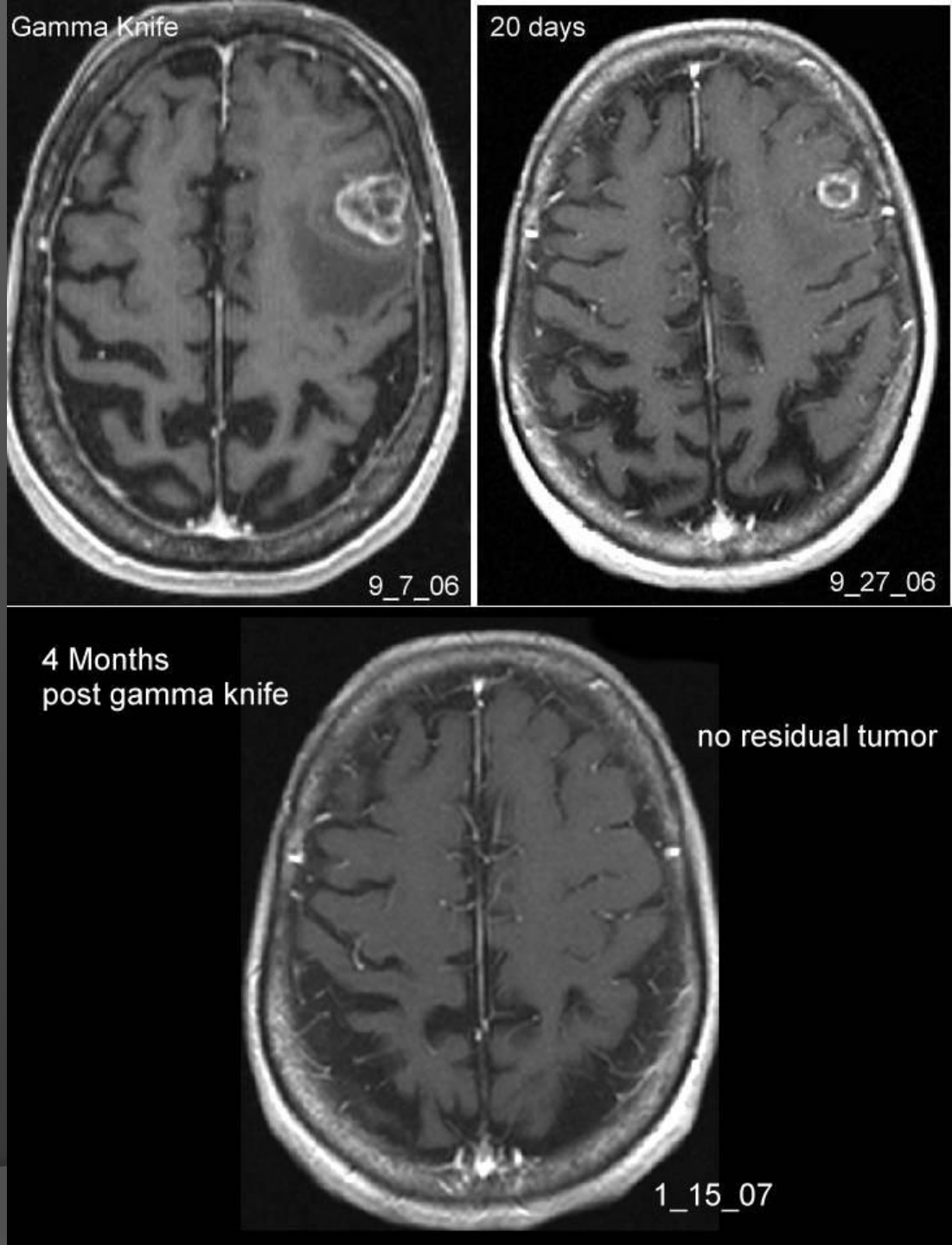
Treatment	Median Survival	Local Failure
Whole brain external	8 – 15 w	52%
surgical resection	33 – 38 w	20%
rasdiosurgery	44 w	14%

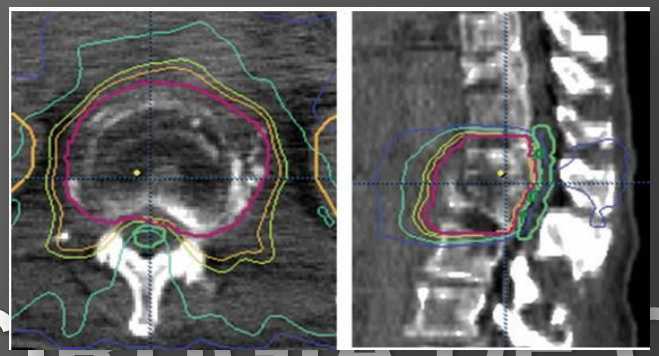
METASTASIS CEREBRAL

RADIOTERAPIA EXTERNA

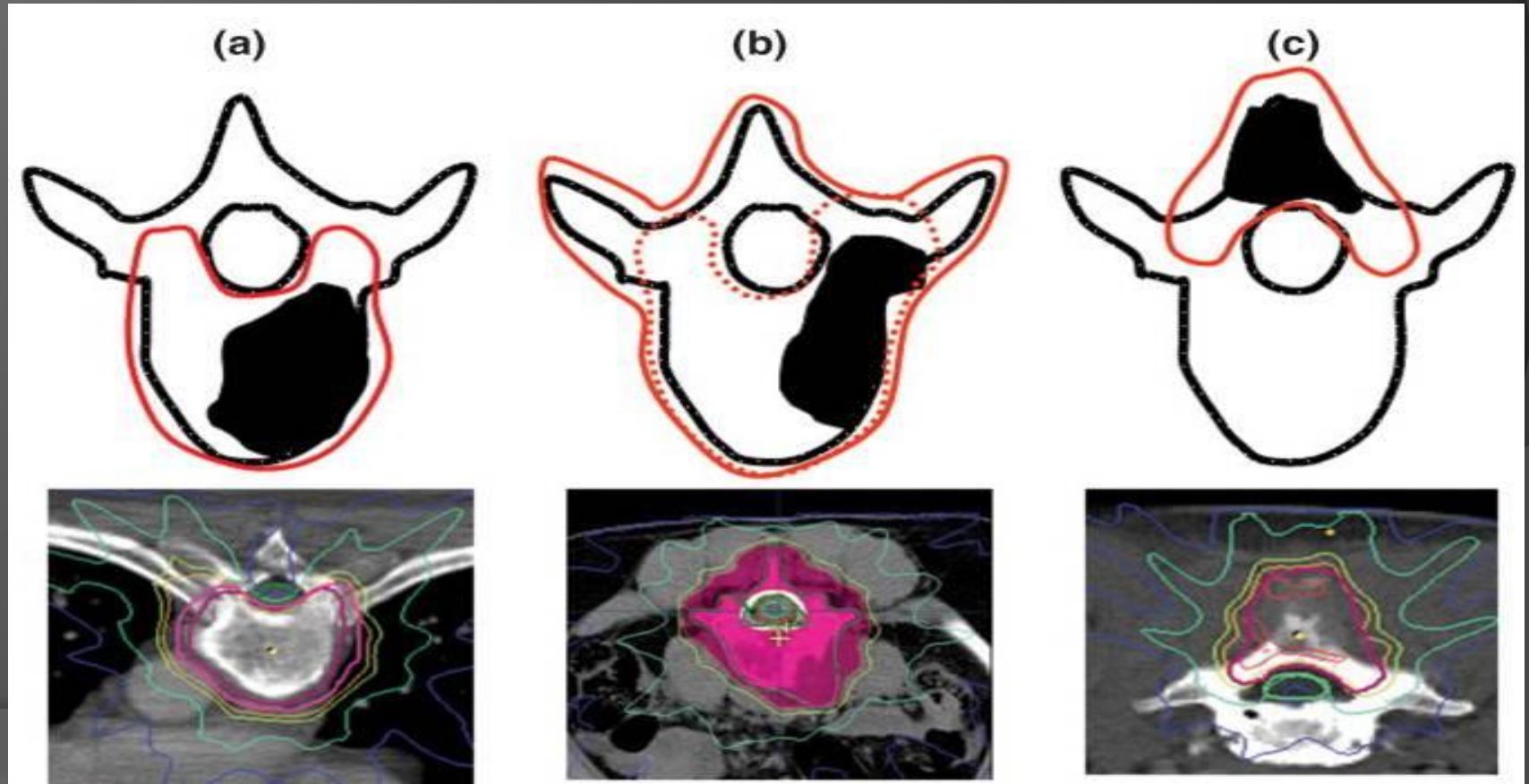
METASTASIS

CEREBRAL RADIOCIRUGIA





RADIOCIRUGIA DE CUERPO VERTEBRAL

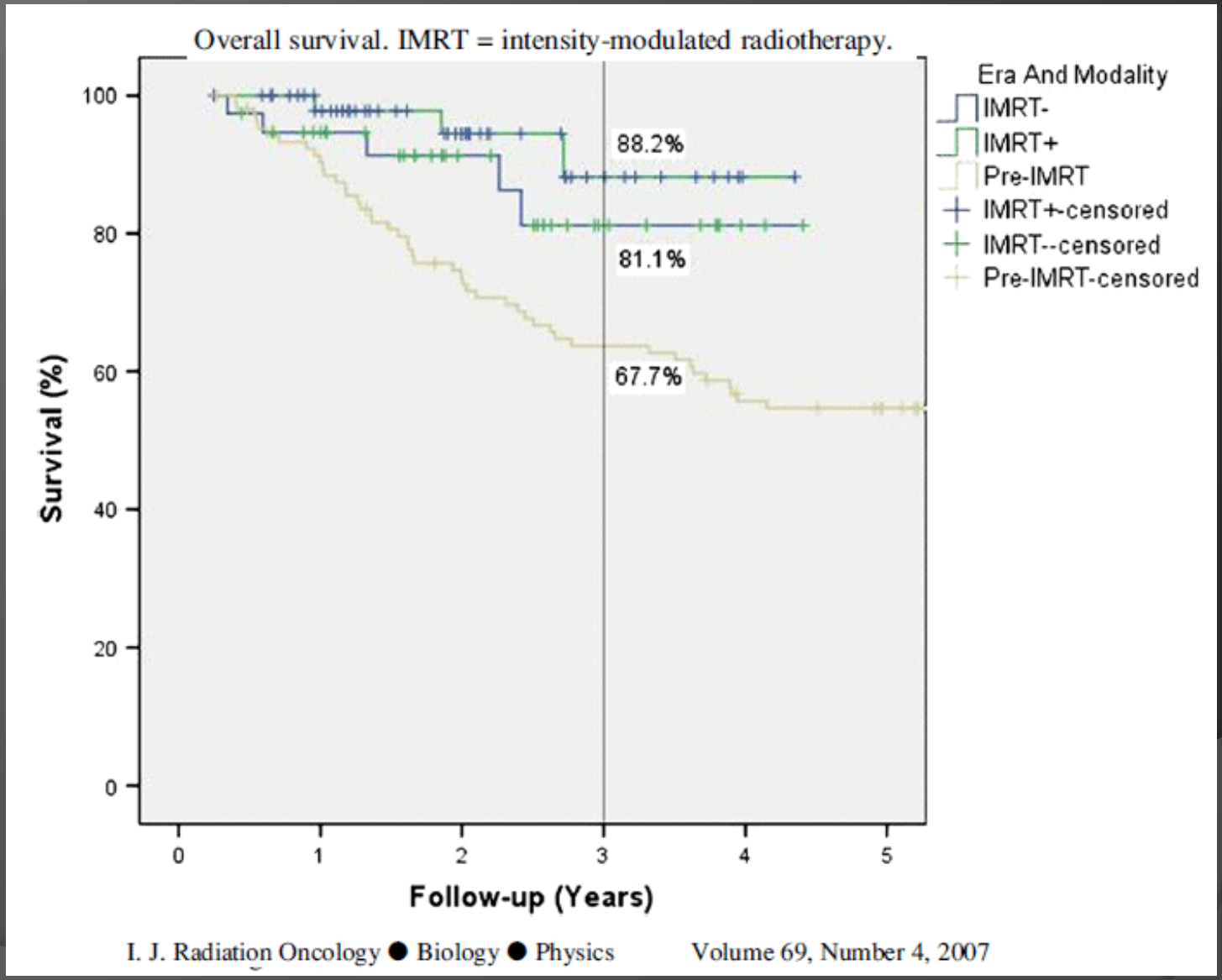


TUMORES DE CABEZA Y CUELLO.

Study	Number of patients		Endpoint	IMRT group	Non-IMRT group	p	Strength of endpoint
	IMRT	Non-IMRT					
Nasopharyngeal carcinoma							
Pow (2006)[4]	24/25*	21/26*	Primary:				
			mean SWS at 12 months (mL/min)	0·27	0·05	<0·05†	Cii
			Secondary:				
			mean SPS at 12 months (mL/min)	0·09	0·00	<0·05†	Cii
			Mean overall health status at 12 months‡	65·7	58·7	>0·05	Ci
			Mean general health at 12 months§	63·9	63·5	>0·05	Ci
			Mean speech problems at 12 months¶	3·2	10·1	<0·05†	Ci
			Mean sticky saliva at 12 months¶	40·3	66·7	<0·05†	Ci
			Mean swallowing at 12 months¶	6·6	10·7	<0·05†	Ci
Wolden (2006)[5]	74	35	3-year local control, %	91	79	0·11	D
Fang (2007)[7]	52	185	Mean overall health status§	64	61	>0·05	Ci
			Mean speech problem¶	12	12	>0·05	Ci
			Mean sticky saliva¶	34	35	>0·05	Ci
			Mean swallowing¶	16	22	>0·05	Ci
Hsiung (2006)[8]	16	16	Mean parotid MER, %	23·3	0·6	0·001†	Cii
			Xerostomia (G0/G1/G2/G3), n	2/6/8/0	0/0/1/15	NA	Cii

IMRT=intensity-modulated radiotherapy. SWS=stimulated whole salivary flow.Cii=quality of life in relation to treatment-induced toxic effects. SPS=stimulated parotid salivary flow. Ci=carefully assessed quality of life. D=indirect surrogates including disease-free survival, progression-free survival, tumour response, local control, and locoregional control. MER=maximal excretion ratio measured by quantitative salivary scintigraphy. G=grade. NA=not available. LPFS=local progression-free survival. RPFS=regional progression-free survival. DMFS=distant metastasis-free survival. NS=not significant. A=overall survival. Strength of endpoint of each study was classified according to the modified Levels of Evidence for Human Studies of Cancer Complementary and Alternative Medicine PDQ. *Included/randomised for analyses. †Statistically significant. ‡Assessed by the European Organisation for Research and Treatment of Cancer core questionnaire (EORTC QLQ-C30). A higher score indicates better functioning. §Assessed by the Medical Outcomes Short Form-36 items Health Survey. A higher score indicates better functioning. ¶Assessed by the EORTC Head-and-Neck module 35 (EORTC QLQ-H&N35). A higher score indicates a more severe symptoms. ||Radiotherapy technique was not a significant factor on multivariate analysis. **33 patients were assessed for late toxic effects. ††The grade of ocular toxicity was not explicitly reported. ‡‡Conventional/3D-conformal radiotherapy.

Mejora de la sobrevida en Cáncer de Cabeza y cuello con IMRT



Int. J. Radiation Oncology Biol. Phys., Vol. 60, No. 5, pp. 1440–1450, 2004

0360-3016/04/$–see front matter

CLINICAL INVESTIGATION **Head and Neck**

TREATMENT OF NASOPHARYNGEAL CARCINOMA WITH INTENSITY-MODULATED RADIOTHERAPY: THE HONG KONG EXPERIENCE

MICHAEL K. M. KAM, F.R.C.R.,* PETER M. L. TEO, F.R.C.R.,† RICKY M. C. CHAU, M.SC.,* K. Y. CHEUNG, PH.D.,* PETER H. K. CHOI, F.R.C.R.,* W. H. KWAN, F.R.C.R.,* S. F. LEUNG, F.R.C.R.,* BENNY ZEE, PH.D.,* AND ANTHONY T. C. CHAN, M.D.*

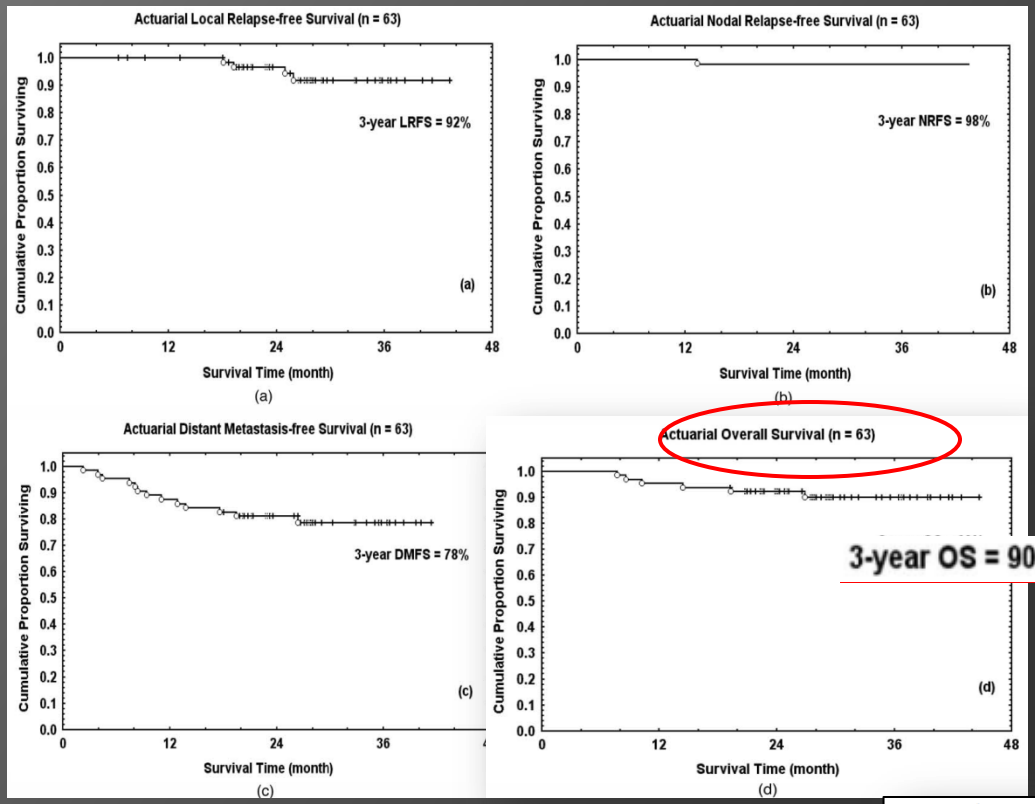


Table 4. Frequency of acute toxicity (Radiation Therapy Oncology Group acute radiation morbidity scoring criteria)

Grade	0	1	2	3	4
Xerostomia	—	16 (25%)	47 (75%)	—	—
Skin reaction	—	35 (57%)	22 (36%)	4 (7%)	—
Dysphagia	—	26 (43%)	27 (44%)	8* (13%)	—
Mucositis	—	5 (8%)	31 (51%)	25 (41%)	—

* Six patients required hospitalization, and five of them required tube feeding.

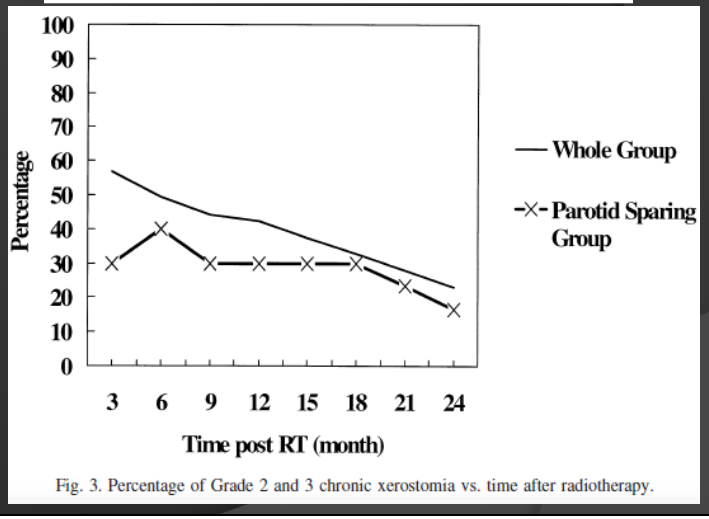


Fig. 3. Percentage of Grade 2 and 3 chronic xerostomia vs. time after radiotherapy.

Table 5. Frequency of late radiation therapy treatment toxicity (Radiation Therapy Oncology Group late radiation morbidity scoring criteria)

Grade	0	1	2	3	4
Hearing	44 (71%)	9 (14.5%)	1 (1.6%)	8 (12.9%)	—
Vision	63 (100%)	—	—	—	—
Swallowing	56 (90.3%)	3 (4.8%)	1 (1.6%)	2 (3.2%)	—
Skin	33 (53.2%)	28 (45.1%)	1 (1.6%)	—	—
Neck fibrosis	27 (43.5%)	28 (45.2%)	6 (9.7%)	1 (1.6%)	—

TUMORES DE CABEZA Y CUELLO.

Función salival y Xerostomia.

- **Prince of Wales Hospital; 2007** (Hong Kong)(2001-2003) -- "Prospective randomized study of IMRT on salivary gland function in early-stage nasopharyngeal carcinoma patients."
- (Kam MK, J Clin Oncol. 2007 Nov 1;25(31):4873-9.)
  - Randomized. 60 patients with T1-2bN0-1 nasopharynx.
  - **Arm 1)** IMRT 66 Gy (CTV=GTV + 1cm; at-risk anatomic sites; LN Levels IB-II, LN upper Level V, LN retropharyngeal; PTV=CTV+3mm), lower neck LN+ 66 Gy anterior field, LN- 54-60 Gy + intracavitary BT boost VS **Arm 2)** 66 Gy 2D + intracavitary BT boost
  - Outcome: observer-related severe xerostomia IMRT 39% vs. 2D-RT 82%,
  but no difference in patient-reported feeling of xerostomia
  - Conclusion: **IMRT superior in preserving objective parotid function, but no difference in patient-reported benefit**
  - Editorial : Observer-rated scoring underestimates patient reports and has low agreement among various observers. Suspect sparing of parotid alone not sufficient. Parotid gland produces saliva without mucins (lubricants, bind water, and provide selective permeability barrier). Mucin-secreting glands (e.g. minor salivary glands, submandibular glands) produce <10% saliva but >50% mucins. May need to spare these glands as well for subjective feeling of benefit

Grills, Mangona, et al
William Beaumont Hospital, Detroit
JCO Feb 2010

First published direct comparison of SBRT to any form of surgery for stage I NSCLC

OUTCOMES AFTER STEREOTACTIC LUNG RADIOTHERAPY OR WEDGE RESECTION FOR STAGE I NON-SMALL CELL LUNG CANCER

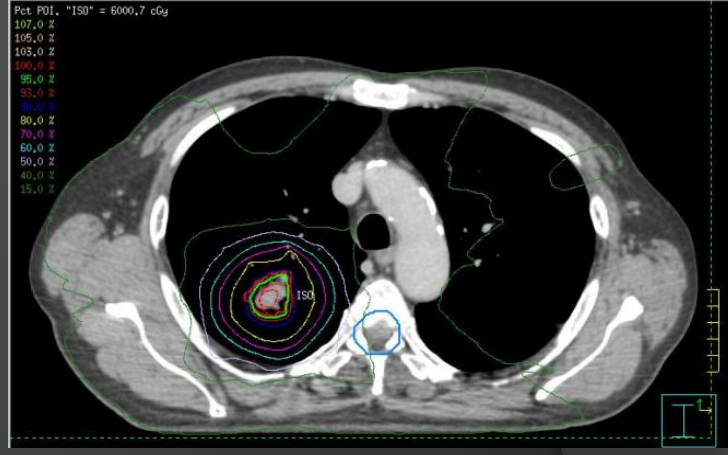
Table 2. Wedge Resection Versus Lung SBRT: 30-Month Outcomes Comparison

Patient Group	% of Patients						
	LR	RR	LRR	DM	FFF	OS	CSS
All patients, n = 124							
SBRT, n = 55	4	4	9	19	77	72	93
Wedge resection, n = 69	20	18	27	21	65	87	94
P	.07*	.34	.16	.96	.37	.01	.53
Exclude pT4, synchronous primary, no biopsy, n = 110							
SBRT, n = 52	5	0	5	15	80	70	92
Wedge resection, n = 58	24	18	29	22	61	85	93
P	.05	.07*	.03	.51	.12	.02	.62

Abbreviations: SBRT, stereotactic radiotherapy; LR, local recurrence; RR, regional recurrence; LRR, locoregional recurrence; DM, distant metastasis; FFF, freedom from any failure; OS, overall survival; CSS, cause-specific survival.

*Statistical trend only.

Irradiación localizada de SBRT



Multiple non-coplanar fixed fields

Arcing IMRT (VMAT/RapidArc/Tomotherapy)

Robotic Mounted Linac (cyberknife)

High precision localised radiotherapy for NSCLC

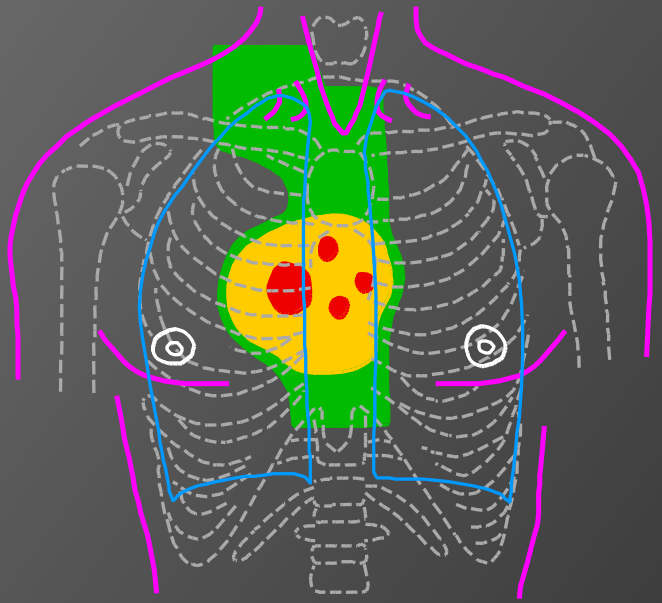
Optimización de la radioterapia

STDF

Tumor

50Gy

60-64Gy

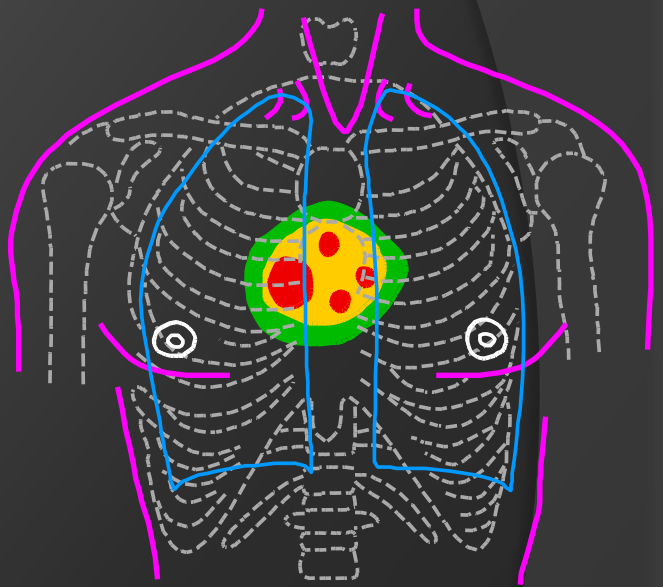


IF

Tumor

50Gy

68-74Gy



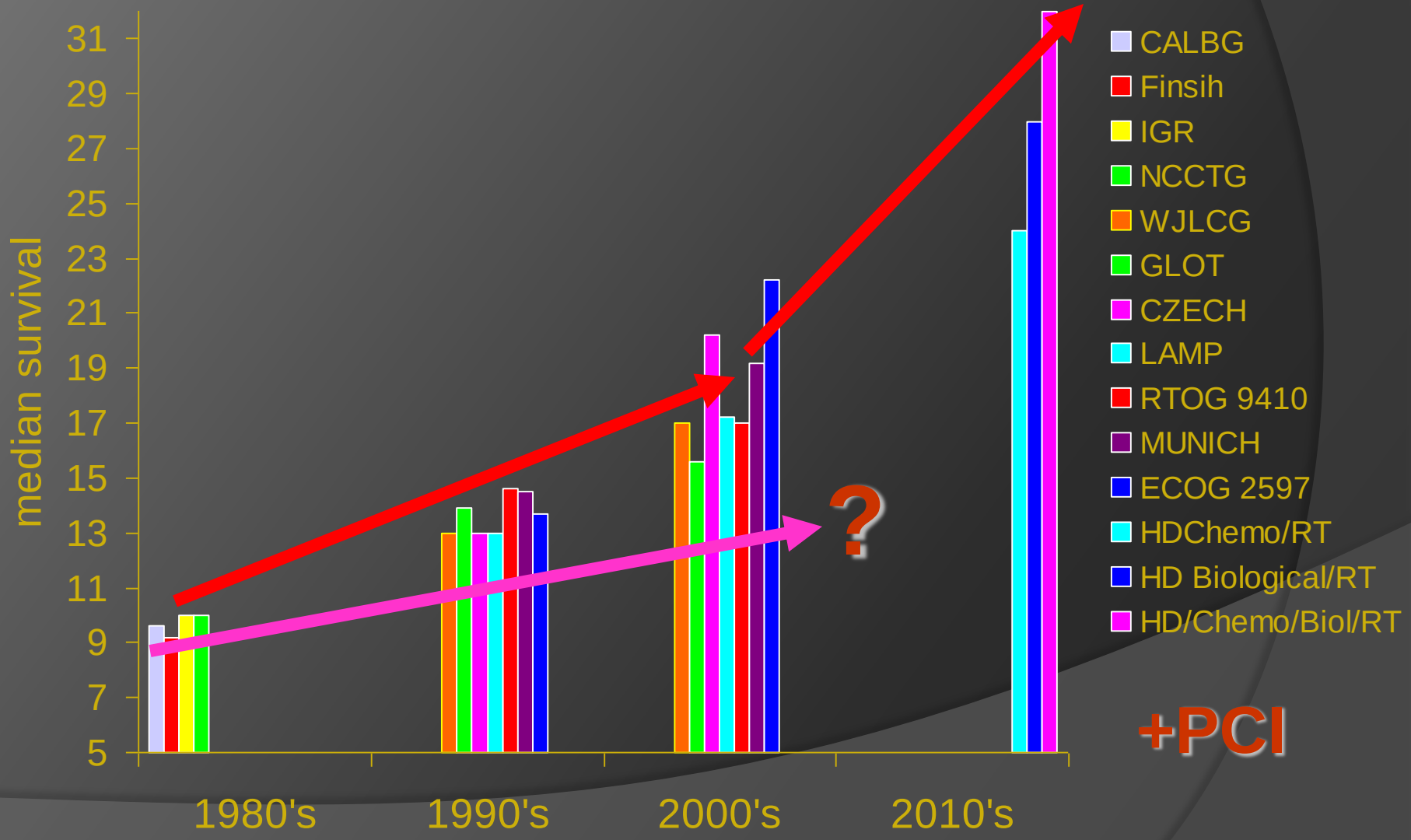
Stage III NSCLC: Chemo→Chemo/RT (200 patients randomized)

	2 yr LF	1yr OS	2 yr OS	3 yr OS
ENI	49	59.7	25.6	19.2
IFRT	41	67.2	38.7	27.3

P = 0.048

Yuan , ASCO 2006, Abstract # 7044

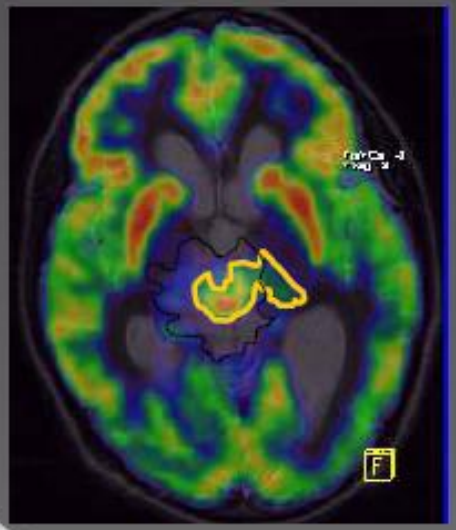
MEJORAS EN LA SOBREVIDA EN CANCER EN CANCER DE PULMON 1980–2010



Planeación de RT y PET-CT

NUEVO CONCEPTO

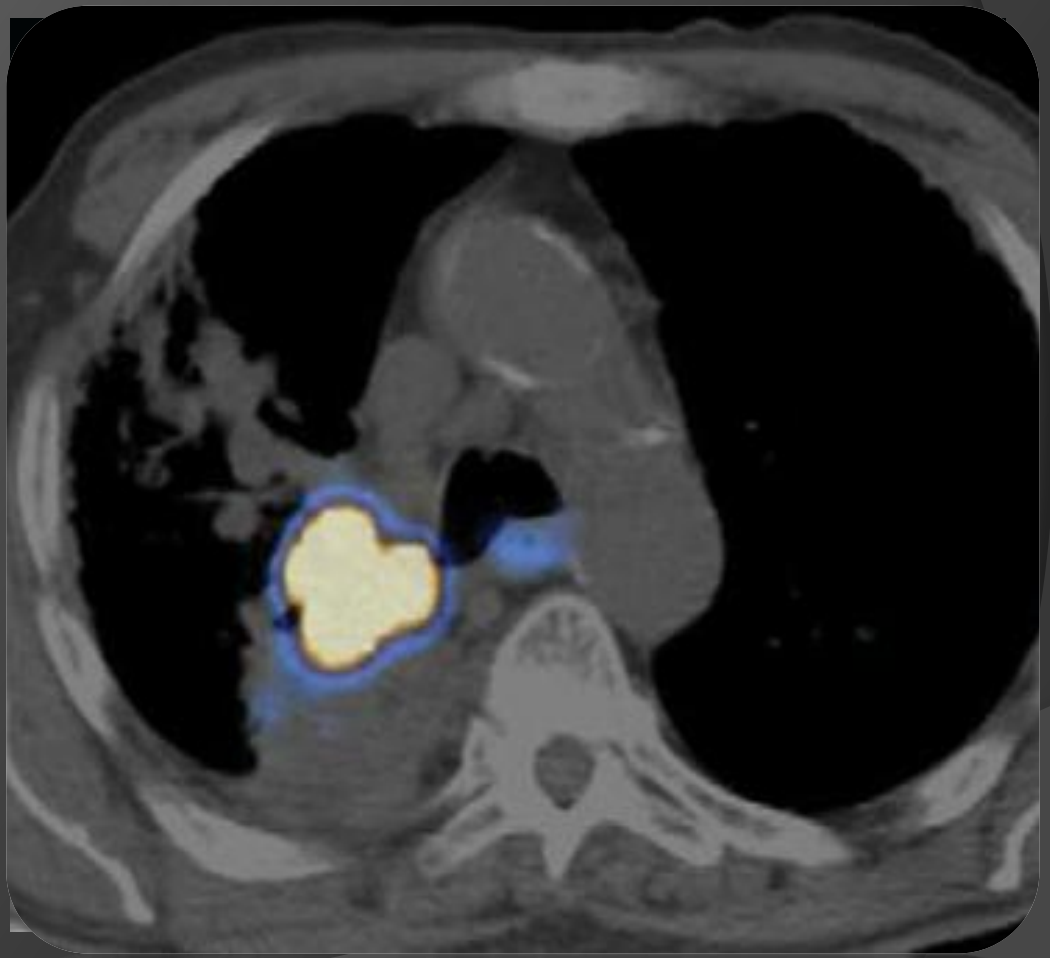
La incorporación del concepto de un volumen tumoral biológico (BTV) en 3D dimensiones, obtenido solo a través de imágenes moleculares provee información específica, molecular y fisiológica a cerca del tumor, que se puede incorporar en la planeación de la radioterapia mejorando la exactitud clínica de la misma y las dosis finales administradas.



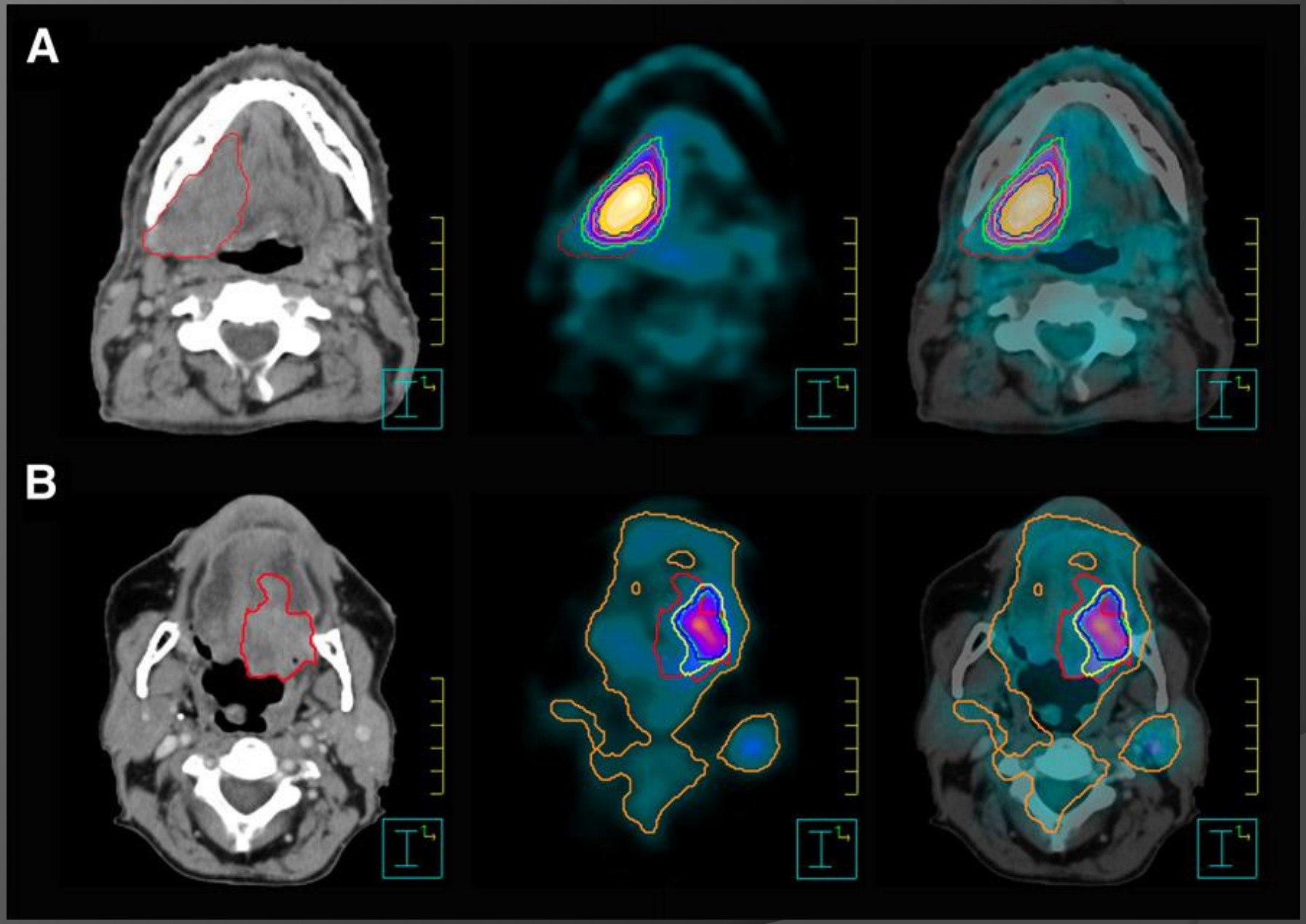
Jeffrey D. Bradley, MD; Carlos A. Perez, MD; Farrokh Dehdashti, MD; and Barry
A. Siegel, MD Implementing Biologic Target Volumes in Radiation Treatment Planning for Non–Small Cell Lung Cancer J Nucl Med 2004; 45:96S–101S. 12.

Delineación del blanco

34 pacientes
17 componente atelectásico
9 cambios en los campos con FDG
6 disminuyó el campo
17 Sin atelectasias
(3 sufrieron cambios)

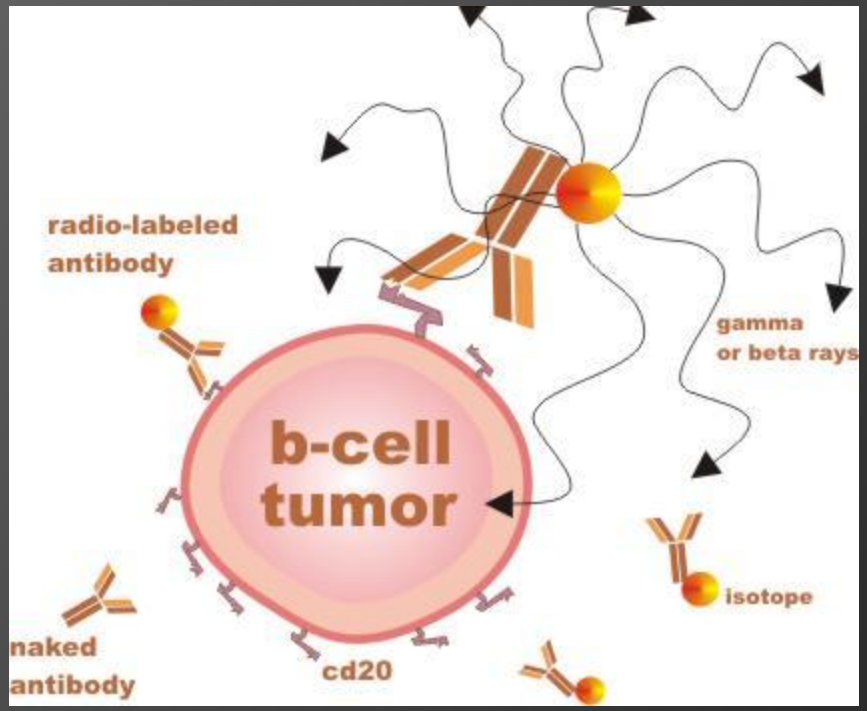


Nestle U et al. Int J Radiat Oncol Biol Phys 1999; 44:593-7



Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 4, pp. 1282–1289, 2007

ANTICUERPO MONOCLONAL RADIO-ACTIVO



monoclonal antibody targets the CD20 antigen, which is found on the surface of B-cell tumors

Radio-active Monoclonal Antibodies

In February 2002, Zevalin was the first radioimmunotherapy to receive FDA approval. Zevalin consists of a monoclonal antibody linked to the radioactive isotope yttrium-90. After infusion into a patient, the monoclonal antibody targets the CD20 antigen, which is found on the surface of B-cell tumors. In this manner, cytotoxic radiation is delivered directly to malignant cells.

On June 30, 2003 announced FDA approval of BEXXAR (Tositumomab and Iodine I 131 Tositumomab)

GRACIAS POR SU ATENCION

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