Radiocirugía Extracraneal - SBRT: actualización desde el punto de vista biológico y clínico

T. Hijal, Department of Radiation Oncology, McGill University

Radioterapia externa con fraccionamiento clásico

ICRU REPORT 50

Prescribing, Recording, and Reporting Photon Beam Therapy

Configuración de haz simple

Campos de radiación más grandes

Fraccionamiento convencional

Distribución de dosis homogénea

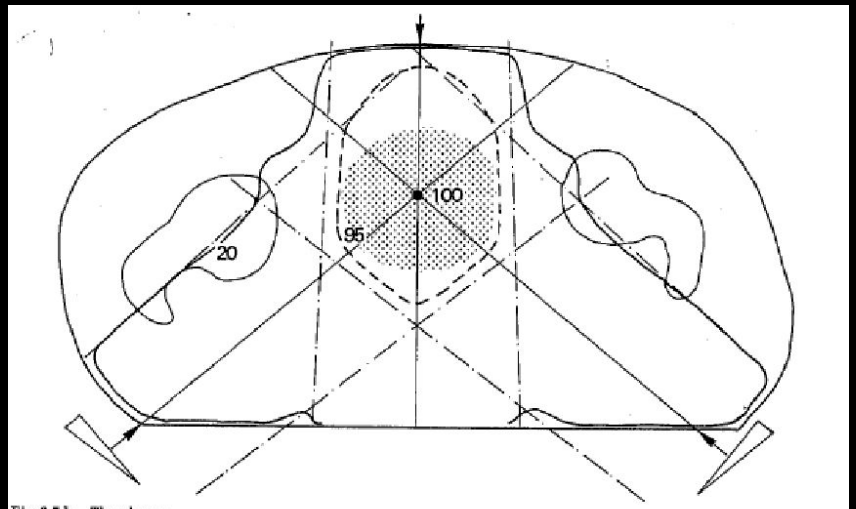


Fig. 2.5.b. Three beams.

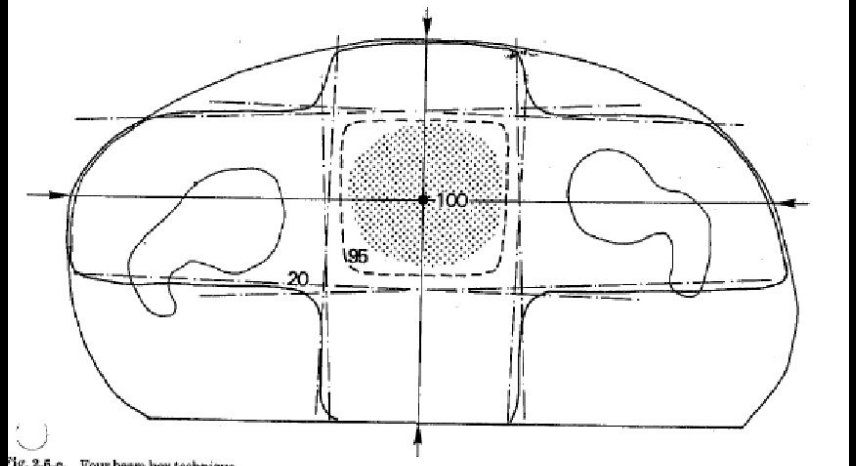


Fig. 2.5.c. Four beam box technique.

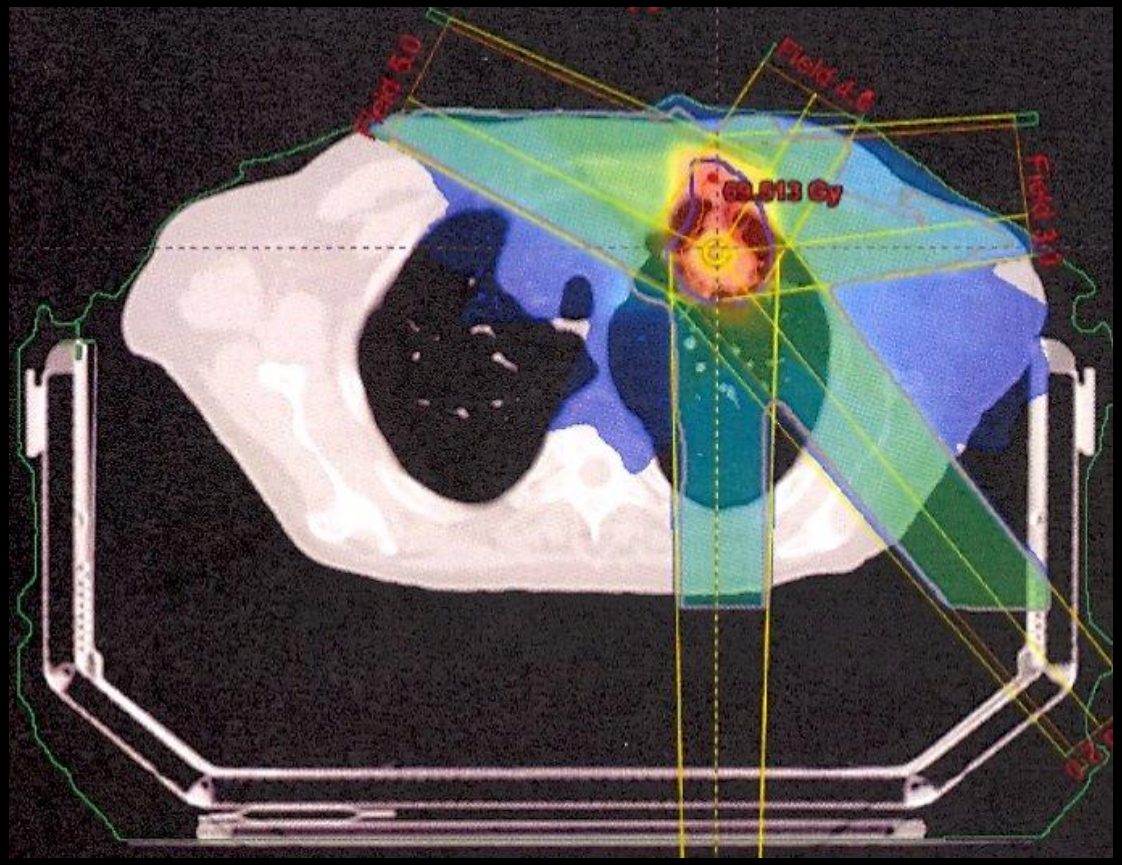
Radioterapia corporal estereotáctica

Múltiples campos coplanares o no coplanares

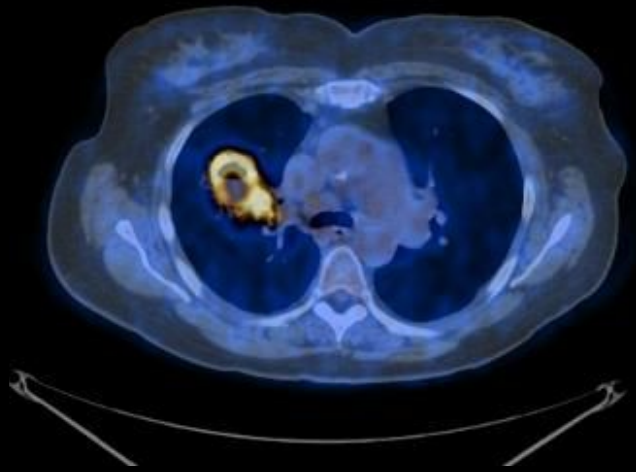
¡Hipofraccionamiento extremo para administrar dosis ablativas!

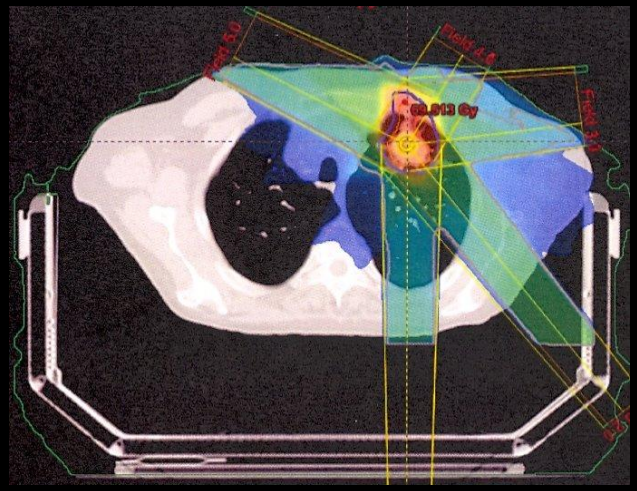
Campos pequeños

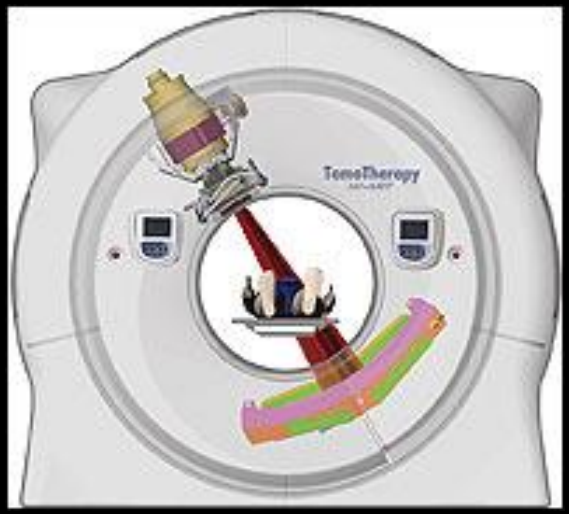
Heterogeneidad deliberada dentro del objetivo



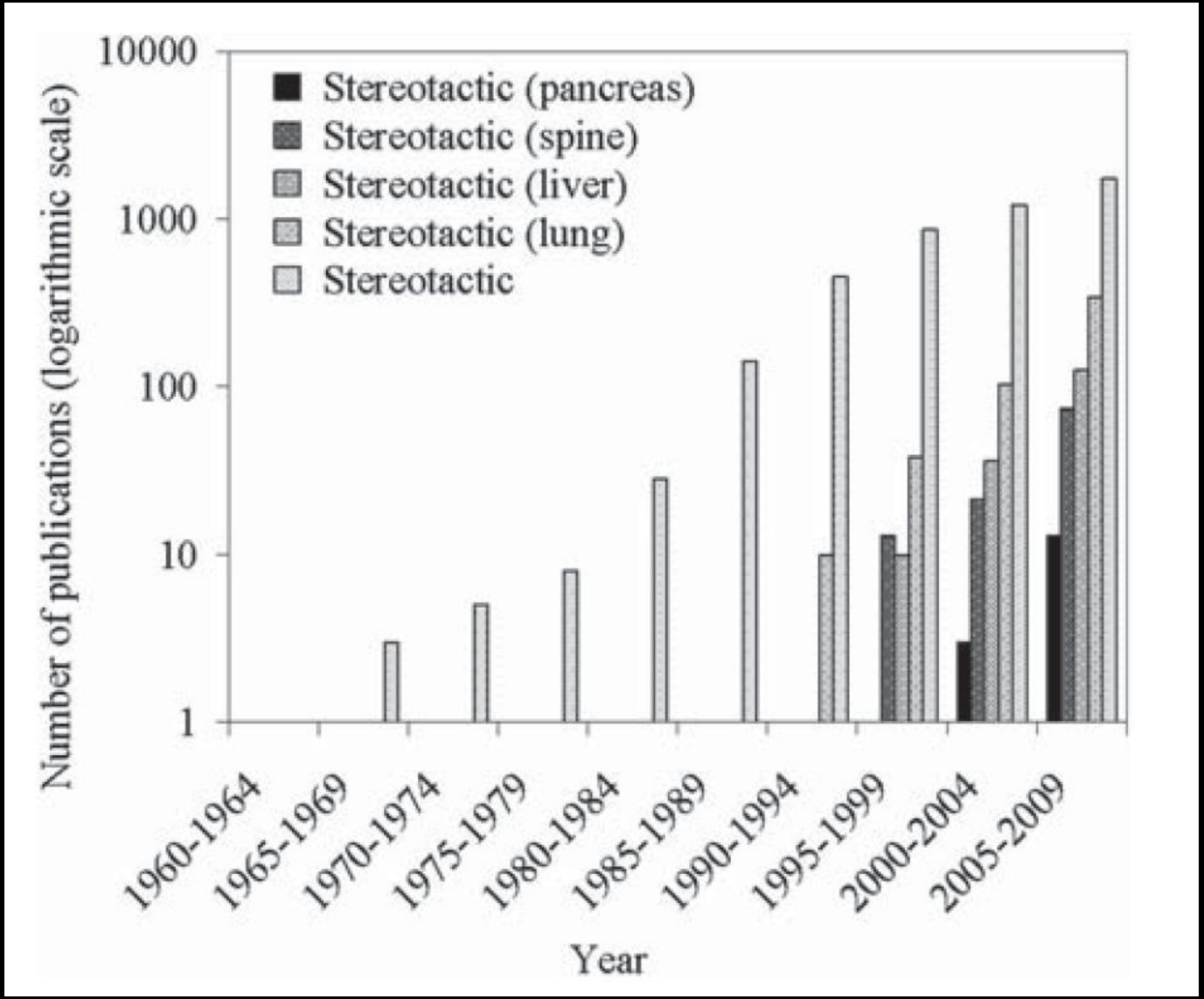
SBRT: ¡Un triunfo de la física médica!







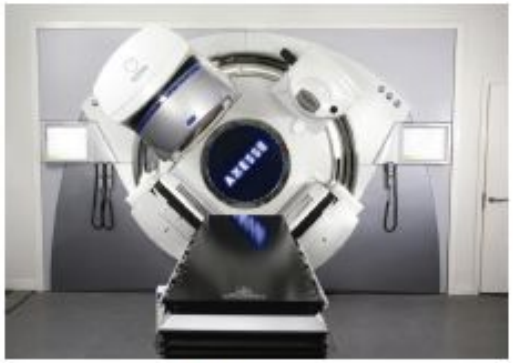
RT estereotáctica: ¡el interés ha crecido exponencialmente!



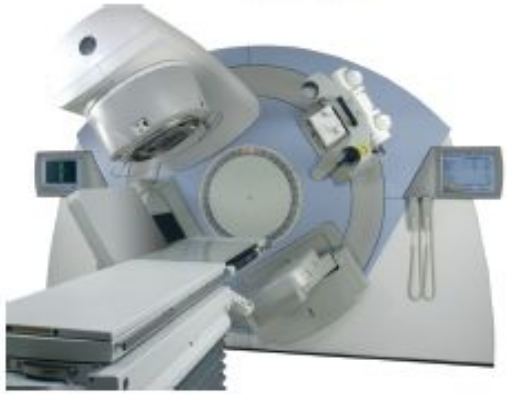
Varios dispositivos capaces de administrar dosis ablativas de radioterapia de haz externo

(a) Novalis Tx

(b) TrueBeam



(c) Elekta Axesse



(d) Elekta Synergy

(e) Cyberknife

(f) TomoTherapy

FIGURE 1: Various treatment devices available for stereotactic ablative radiotherapy.

1. SBRT pulmonar: técnica

2. SBRT pulmonar: efectos secundarios

3. SBRT pulmonar: indicaciones clínicas y evidencia

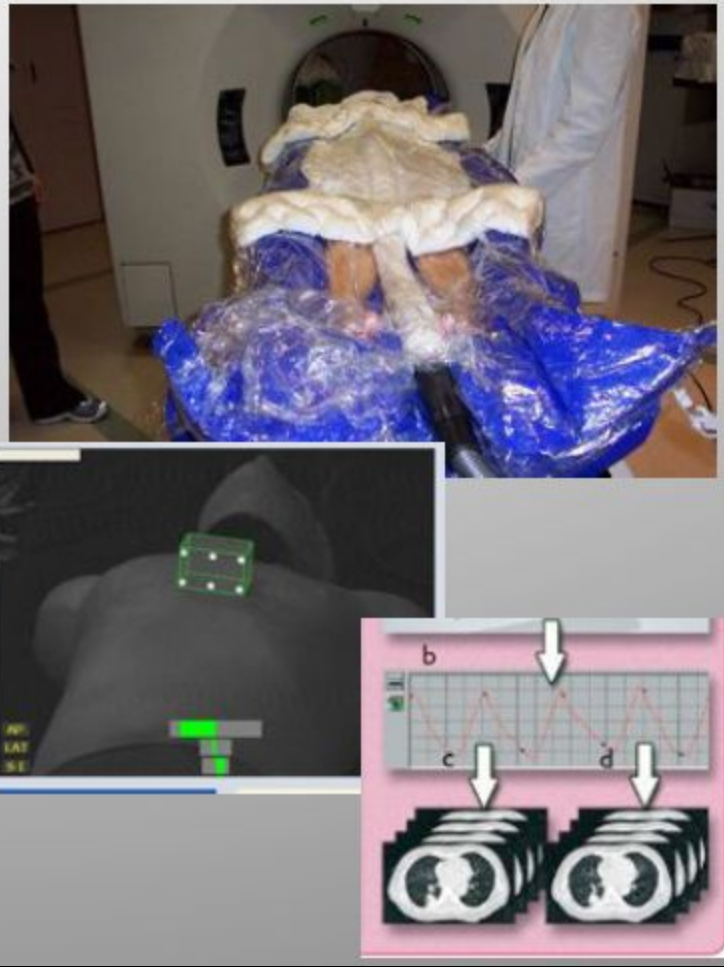
1. **SBRT pulmonar: técnica**

2. **SBRT pulmonar: efectos secundarios**

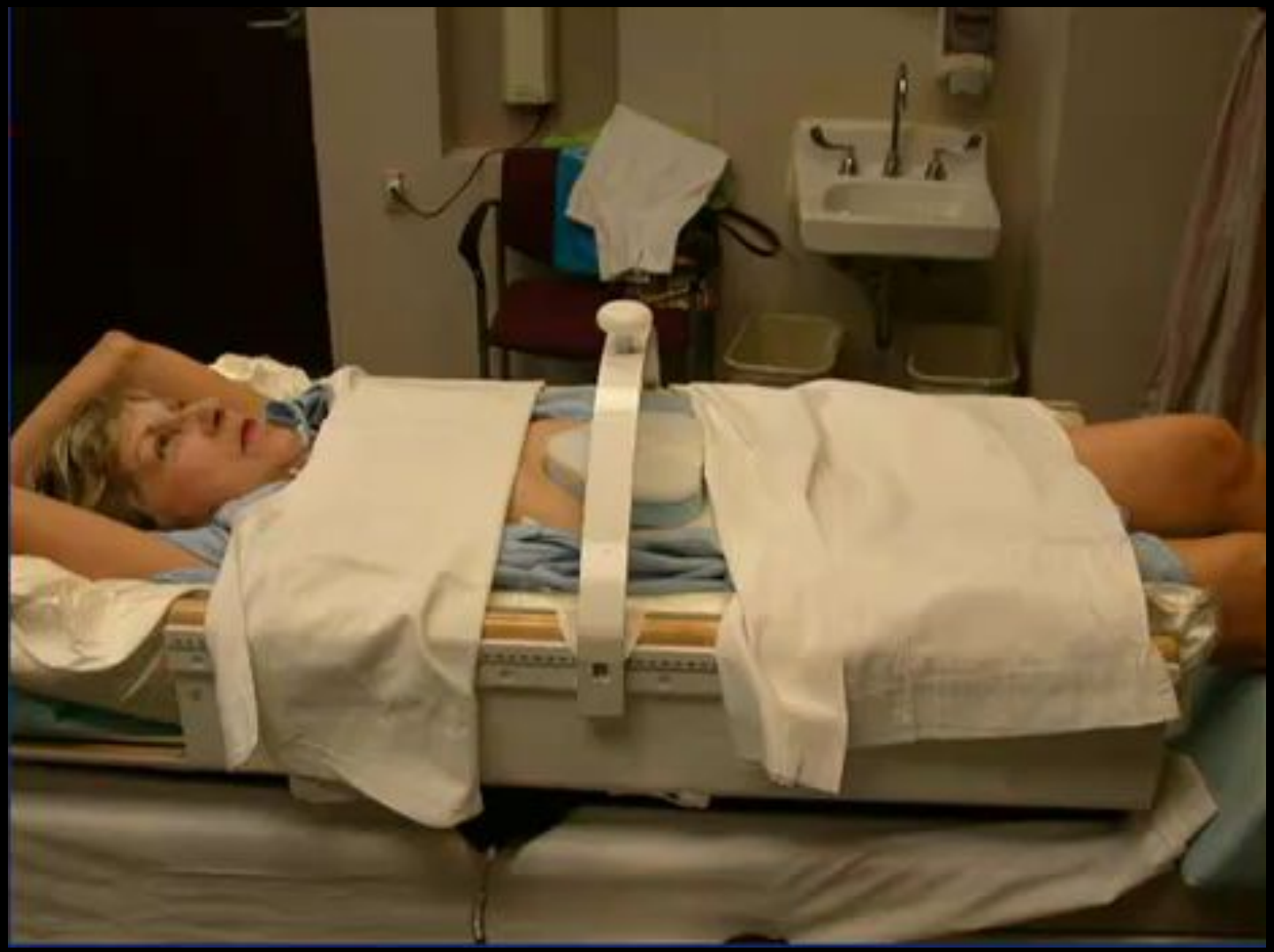
3. **SBRT pulmonar: indicaciones clínicas y evidencia**

Elementos de la técnica SBRT pulmonar: simulación 4D

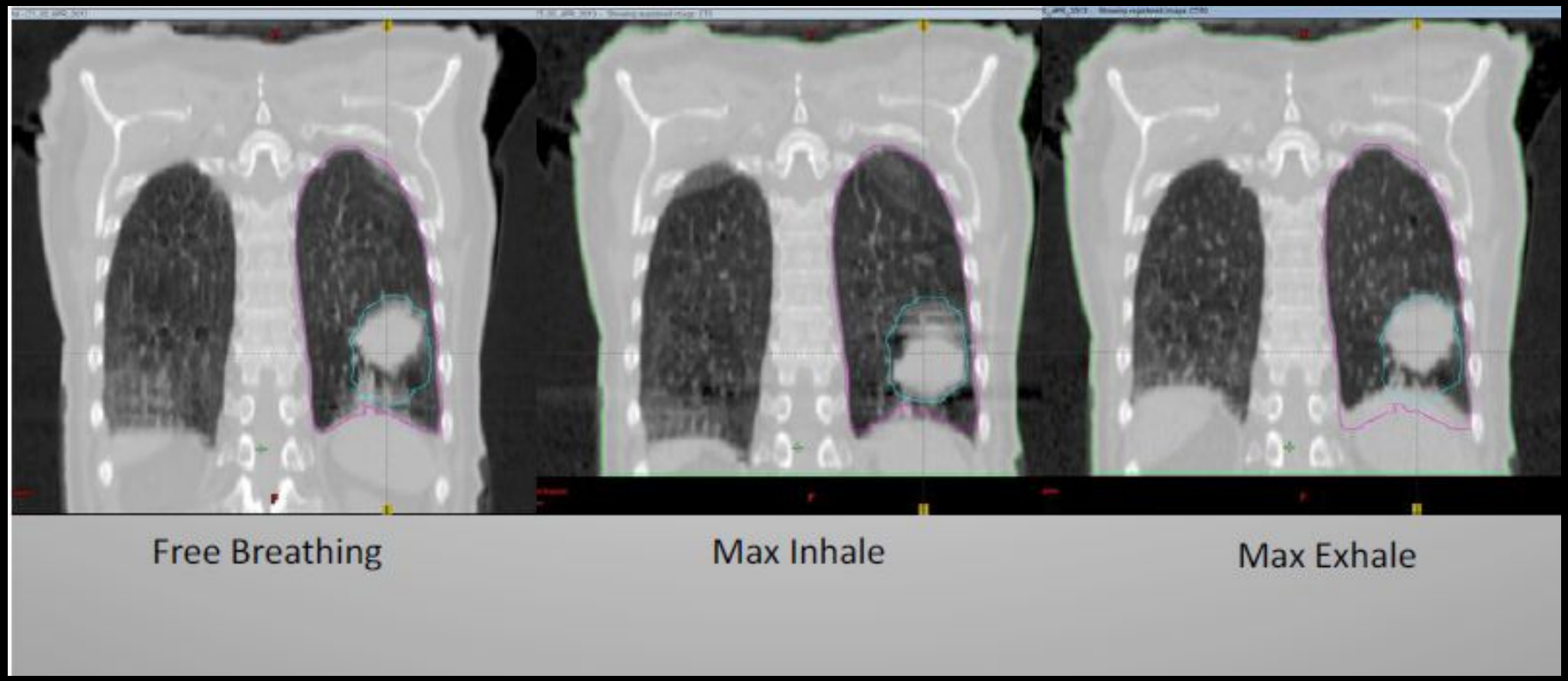
- Patients in BodyFIX
  - Vacuum to 80% - 100%
- 4DCT and free breathing CT acquired
  - 3mm slice width
  - Varian RPM
  - All phases plus MIP reconstructed
  - 0%, 50%, MIP and free breathing scan sent for contouring



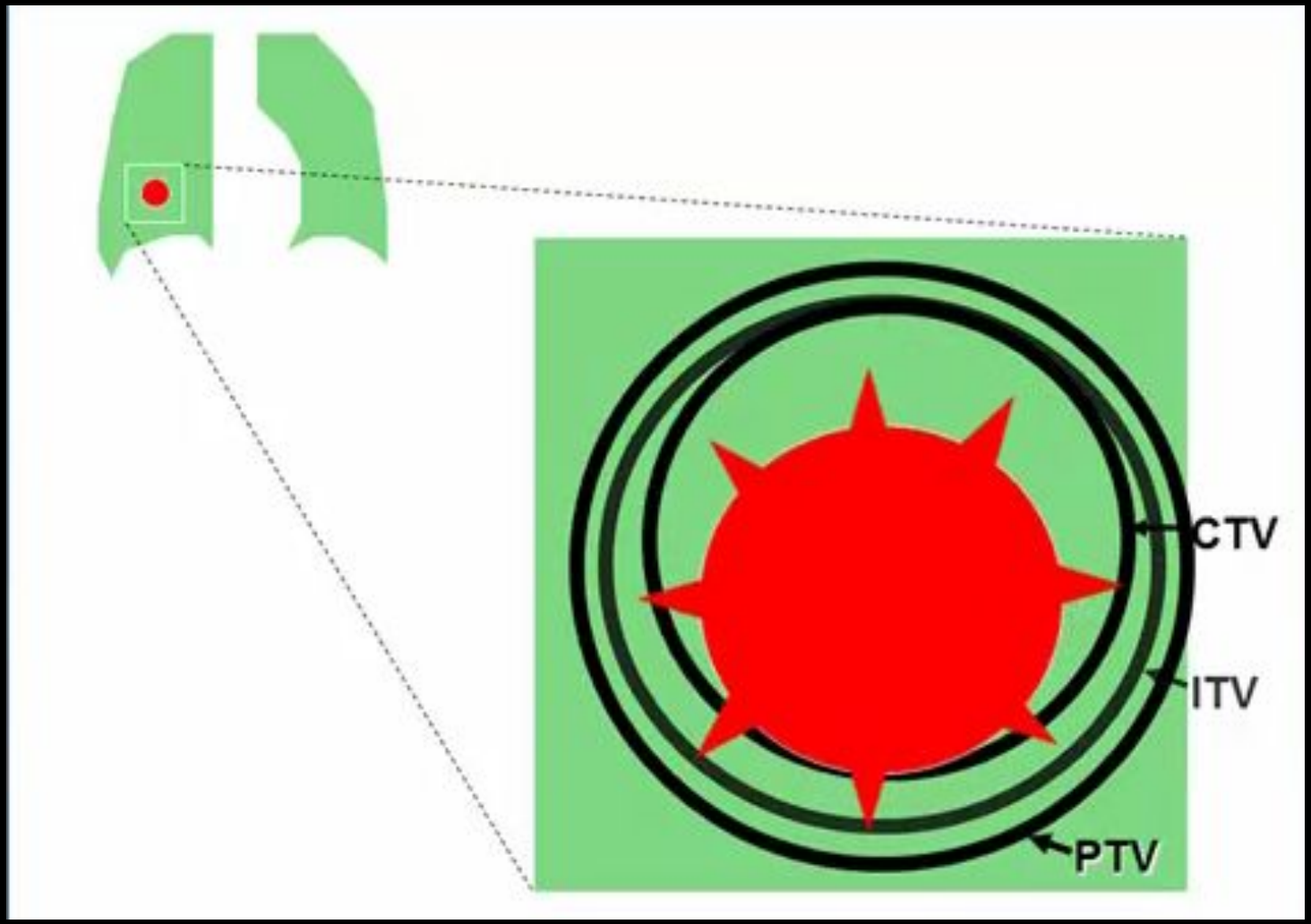
Elementos de la técnica SBRT pulmonar: simulación 4D



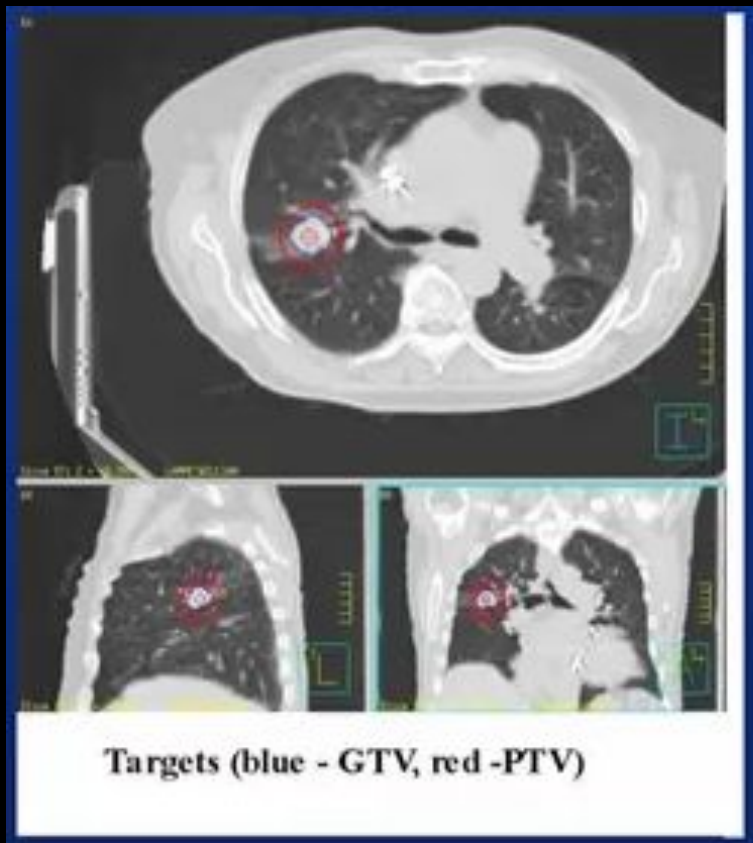
Elementos de la técnica SBRT pulmonar: simulación 4D



Elementos de la técnica SBRT pulmonar: definir los volúmenes



Alta dosis conformacional

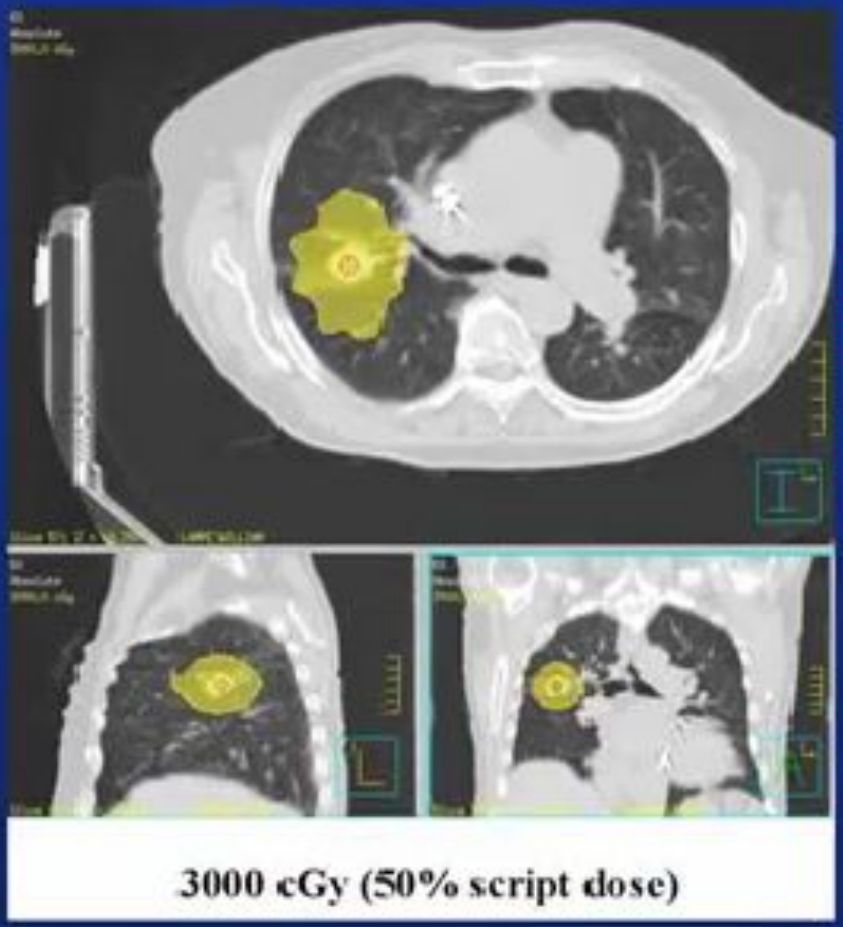


Targets (blue - GTV, red -PTV)

6000 cGy (script dose)

-This constitutes the tumor control (place it well)
- Being conformal is easy – especially with many beams or arcs

Dosis intermedia compacta

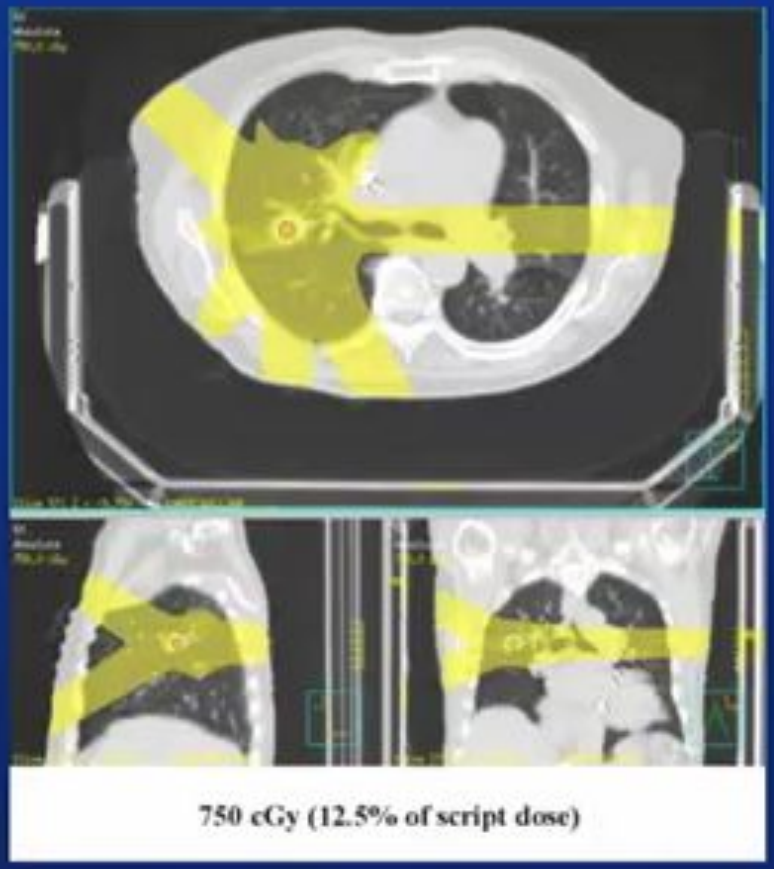


3000 cGy (50% script dose)

This is the hardest part of the SBRT process and distinguishes a good plan from a poor plan!

This accounts for toxicity. All of this dose is in normal tissues
Infinite possibilities – some much more toxic than others

Gran región de dosis baja



- SBRT (and radiosurgery) Assumption: A little dose to a lot of normal tissue is better than a lot of dose to a little normal tissue

Extreme Polarization of Dose

Targets (blue - GTV, red -PTV)

Conventional Radiotherapy

6000 cGy (script dose)

SBRT

1. SBRT pulmonar: técnica

2. SBRT pulmonar: efectos secundarios

3. SBRT pulmonar: indicaciones clínicas y evidencia

Toxicity

Radiotherapy and Oncology 93 (2009) 402–407

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Lung cancer SBRT

Co-morbidity index predicts for mortality after stereotactic body radiotherapy for medically inoperable early-stage non-small cell lung cancer

Neil Kopek [a,*], Merete Paludan [a], Jørgen Petersen [b], Anders Traberg Hansen [b], Cai Grau [a], Morten Høyer [a]

[a] *Department of Oncology, Aarhus University Hospital, Denmark*
[b] *Department of Medical Physics, Aarhus University Hospital, Denmark*

Toxicity

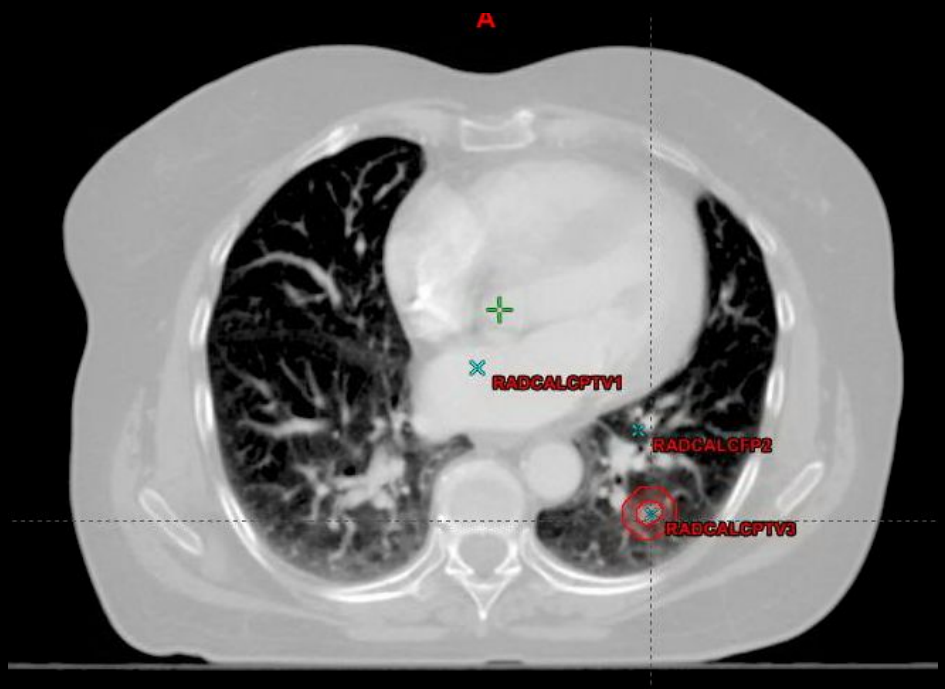
Table 3
Adverse events (CTCAEv.3) registered as worst grade above baseline over the entire follow-up period.

Parameter	1	2	3	4	Any grade
Performance status[a]	6	15	13	3	37
Pain MSK	5	2	1	0	8
Pain PULM	10	7	1	0	18
Analgesia[a]	6	5	5	4	20
Dyspnea	12	9	11	0	32
Pulmonary fibrosis	52	2	0	0	54
Pneumonitis/infiltrates	48	1	0	0	49
Atelectasis	31	0	0	0	31
Pleural effusion	4	2	0	0	6
Cough	1	0	1	0	2
Skin erythema	1	1	0	0	2
Skin fibrosis	2	0	0	0	2
Skin hyperpigmentation	0	2	0	0	2
Esophagitis	0	1	0	0	1
Other (fatigue × 2, dysphagia × 1)	2	1	0	0	3
Total	180	48	32	7	267

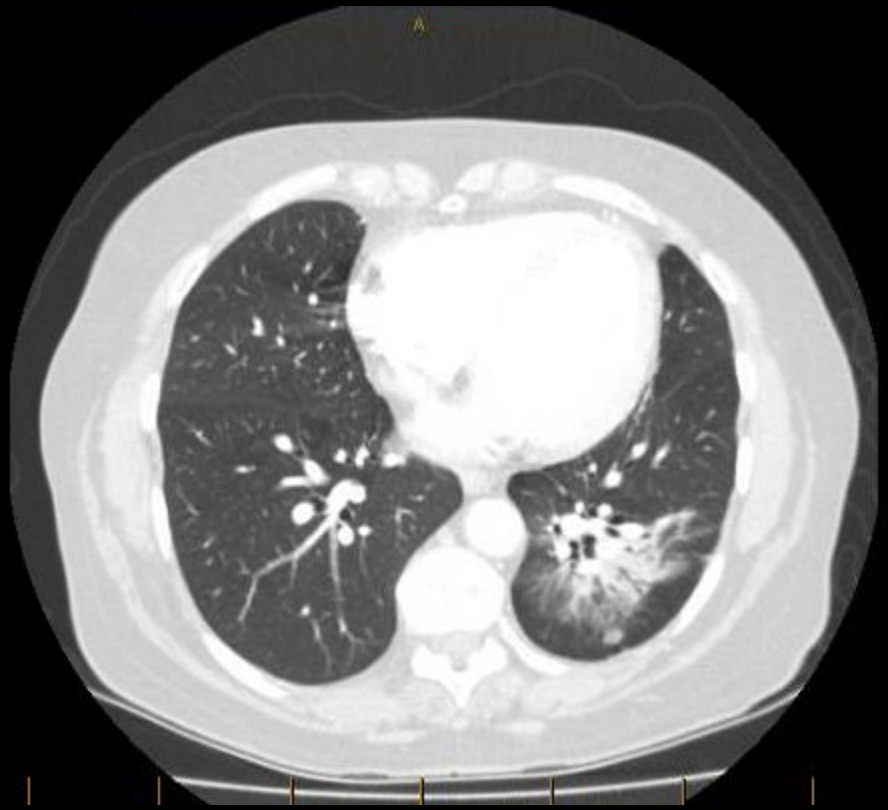
Abbreviations: CTCAEv.3 = Common Terminology Criteria Adverse Events version 3.0; MSK = musculoskeletal; PULM = pulmonary.

[a] World Health Organisation scoring criteria.

Cambios pulmonares después de la radioterapia



Mayo 2016



Sep 2016

Radiotherapy and Oncology 88 (2008) 359–367
www.thegreenjournal.com

Lung cancer SBRT

Stereotactic body radiotherapy for medically inoperable patients with stage I non-small cell lung cancer – A first report of toxicity related to COPD/CVD in a non-randomized prospective phase II study

Pia Baumann[a,*], Jan Nyman[d], Morten Hoyer[e], Giovanna Gagliardi[a], Ingmar Lax[a]
Berit Wennberg[a], Ninni Drugge[d], Lars Ekberg[b], Signe Friesland[a], Karl-Axel Johansson[d]
Jo-Åsmund Lund[f], Elisabeth Morhed[c], Kristina Nilsson[c], Nina Levin[f], Merete Paludan[e]
Christer Sederholm[g], Anders Traberg[e], Lena Wittgren[b], Rolf Lewensohn[a]

[a]Divisions of Oncology and Hospital Physics, Radiumhemment, Karolinska University Hospital, Sweden, [b]Divisions of Oncology and Hospital Physics, Malmö University Hospital, Sweden, [c]Department of Oncology and Radiotherapy, Akademiska University Hospital, Uppsala, Sweden, [d]Department of Oncology and Radiation Physics, Sahlgrenska University Hospital, Gothenburg, Sweden, [e]Divisions of Oncology and Medical Physics, Aarhus University Hospital, Denmark, [f]Department of Oncology, Trondheim University Hospital, Norway, [g]Department of Oncology, Linköping University Hospital, Sweden

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[a]Divisions of Oncology and Hospital Physics, Radiumhemment, Karolinska University Hospital, Sweden, [b]Divisions o Hospital Physics, Malmö University Hospital, Sweden, [c]Department of Oncology and Radiotherapy, Akademiska Uni Uppsala, Sweden, [d]Department of Oncology and Radiation Physics, Sahlgrenska University Hospital, Gothenbur [e]Divisions of Oncology and Medical Physics, Aarhus University Hospital, Denmark, [f]Department of Onco Trondheim University Hospital, Norway, [g]Department of Oncology, Linköping University Hospital, Swe

Ninguna disminución significativa en el FEV1% para el grupo de EPOC

No se observó neumonitis de grado 3 o peor.

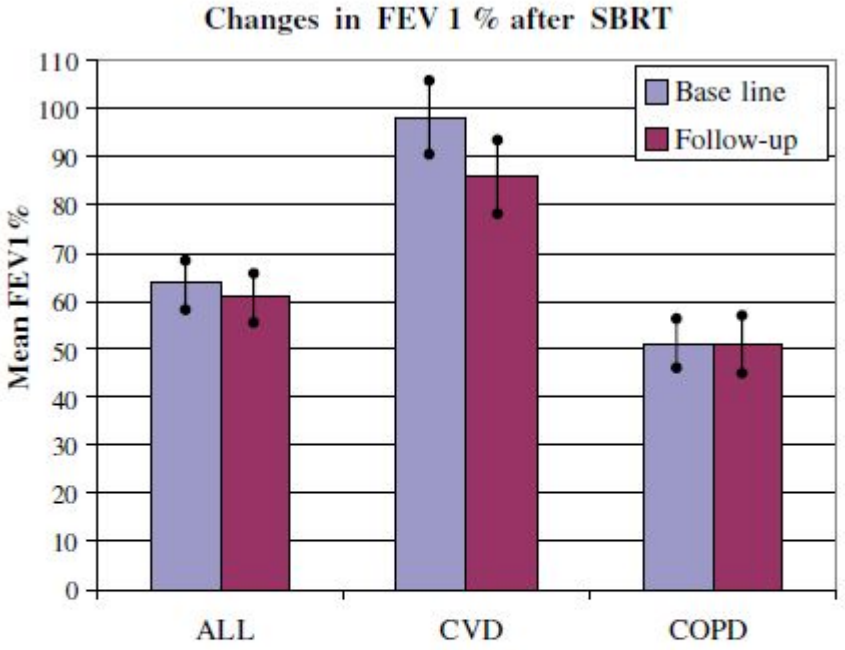

Fig. 2. Changes in objective lung function from baseline to last follow-up, measured as mean FEV1% (forced expiratory volume in 1 second) at baseline and at last recorded follow up, with a 95% confidence interval, in all patients (48 cases), one group with cardiovascular disease (CVD, 14 cases) and one with chronic obstructive pulmonary disease (COPD, 34 cases). The follow up time ranges (month) were as follows; ALL 14.3 (3.0-33.4), CVD 12.1 (8.5-33.4) and COPD 16.2 (3.0-26.5).

Toxicity with central lesions

VOLUME 24 · NUMBER 30 · OCTOBER 20 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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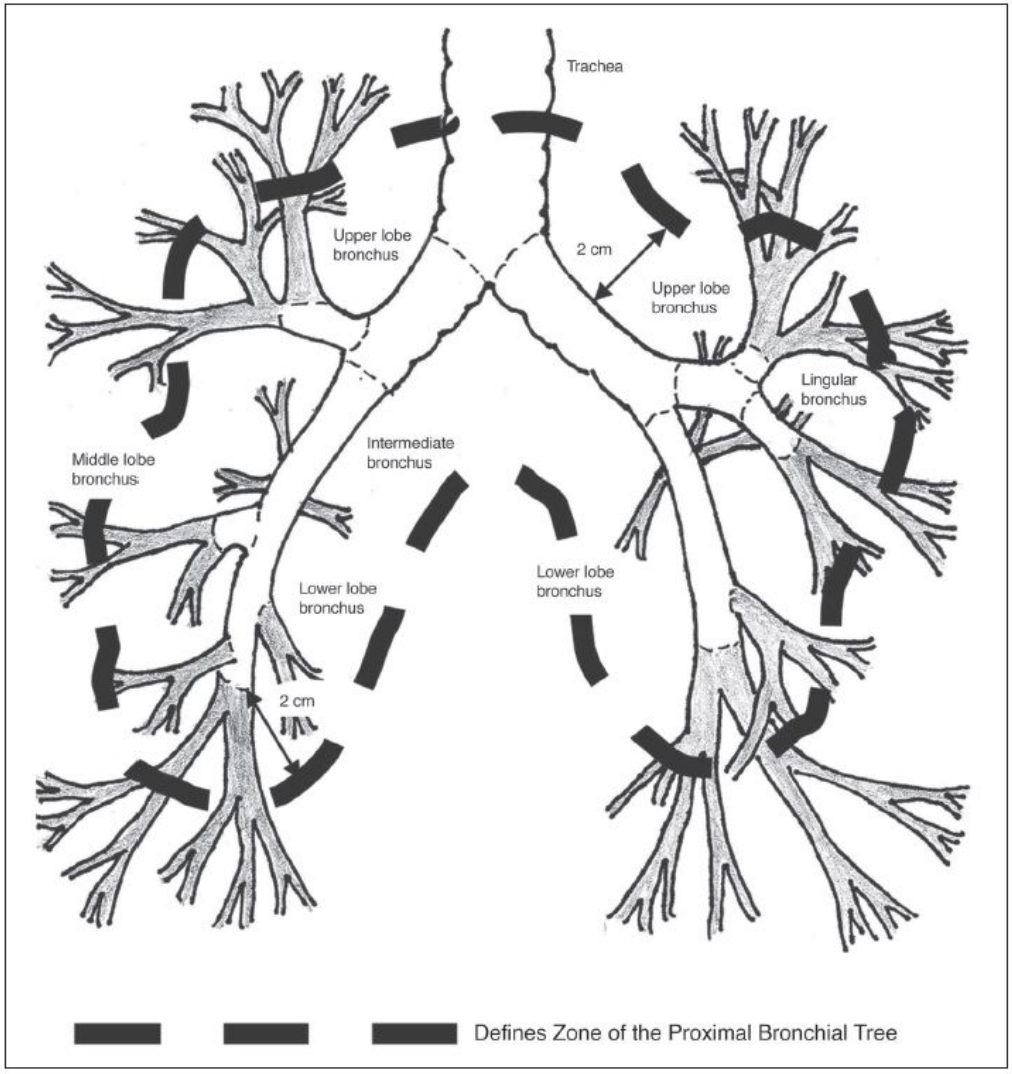

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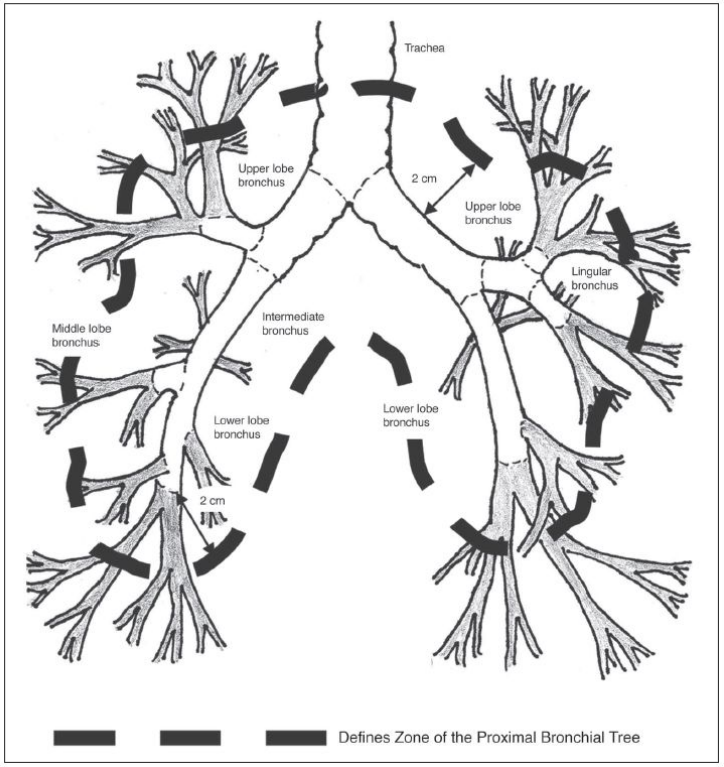


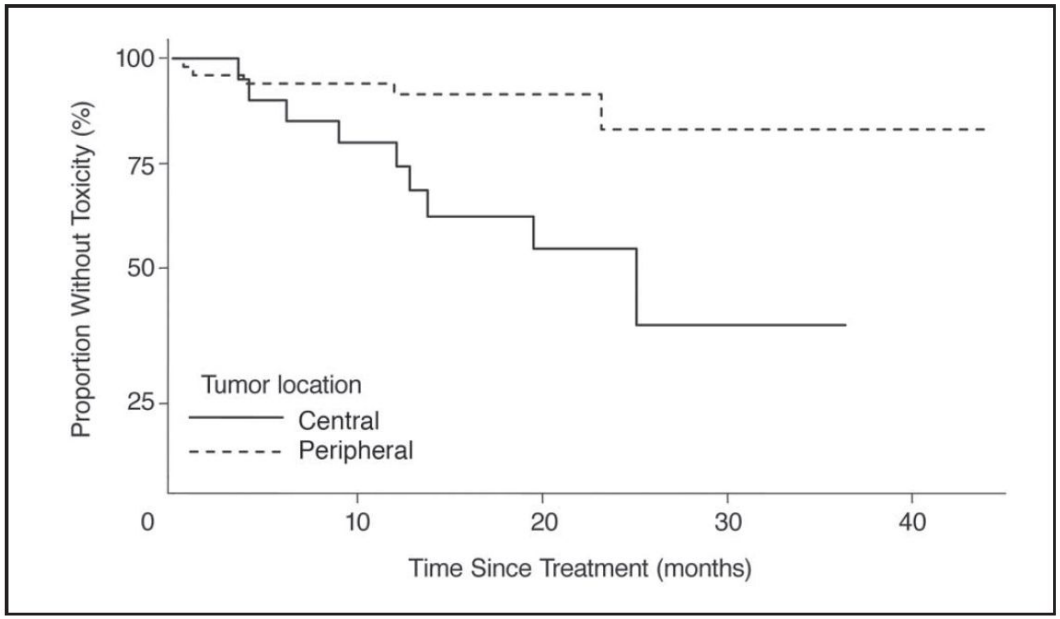
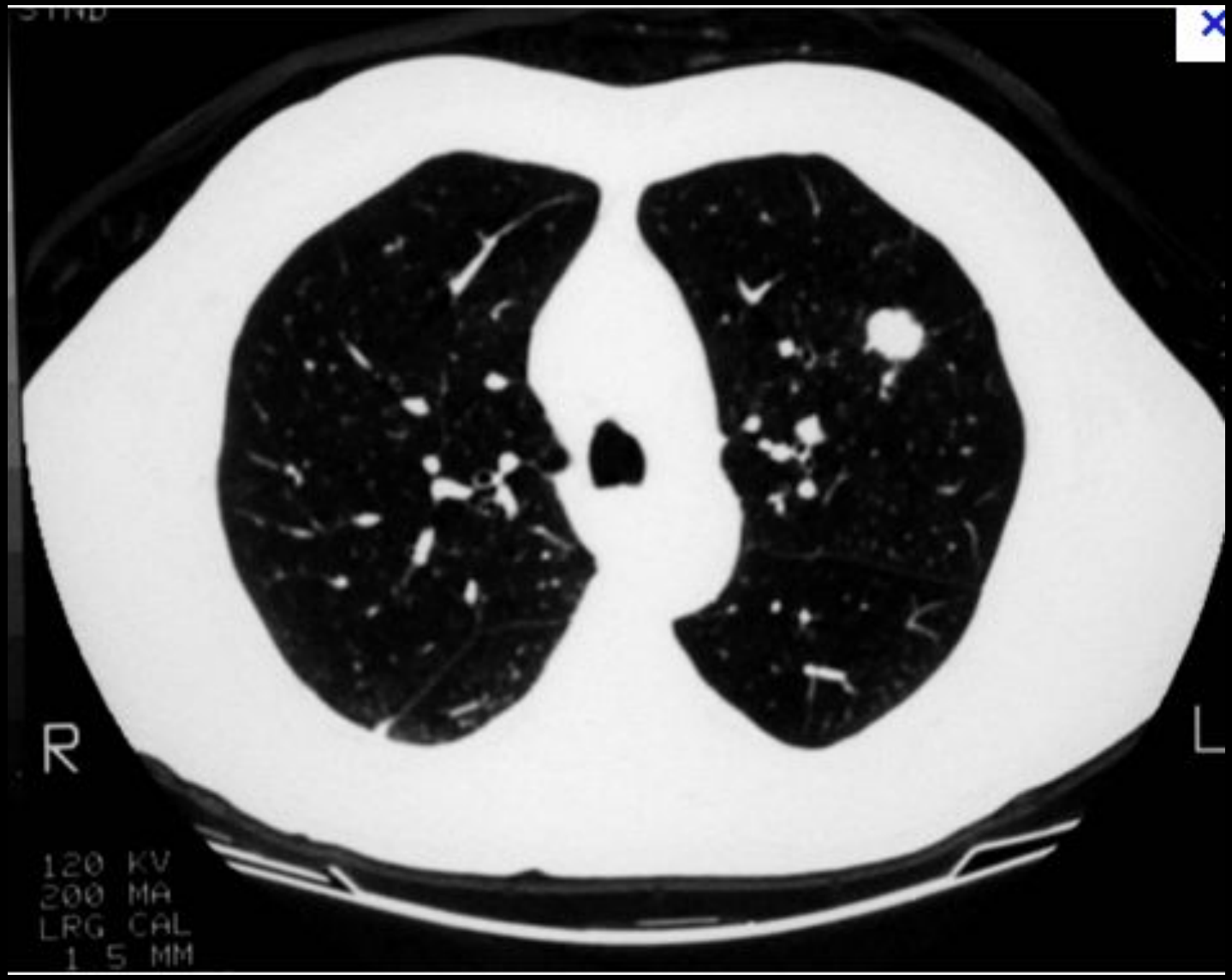


Fig 4. Kaplan-Meier plot of time from treatment until grade 3 to 5 treatment related toxicity comparing patients with tumors in the central (perihilar and central mediastinal) regions from those with more peripheral tumors.

1. SBRT pulmonar: técnica
2. SBRT pulmonar: efectos secundarios
3. SBRT pulmonar: indicaciones clínicas y evidencia

Cáncer de pulmón



Datos no aleatorios para CPCNP de etapa inicial inoperable

Table 1
Selected published studies of SABR in inoperable early stage NSCLC.

Study (year)	Type of study	N	T1-T2	Operability	Initial PET FDG	BED (Gy)	Prescription	FU (m)	Definition of LR	Local control	Distant control	PredLR	LR (NS)	Pred RR	RR (NS)	Pred DR	DR (NS)
Zimmerman (2006) [52]	Prospective phase I/II	68	NA	68 inoperable	Yes	38, 4–84, 37	Isodose 60%	17	Progression of treated lesion	88% (2 years)	NA	NA	NA	NA	NA	NA	NA
Onishi (2007) [10]	Retrospective	257	164/93	99 operable/158 inoperable	No	57–180 (108)	Isocentre	38	Progression of treated lesion	84%	80%	BED<100Gy	Stage IA vs IB	BED<100Gy	Stage IA vs IB	None	BED & Stage
Baumann (2009) [18]	Non randomized Phase II	57	40/17	57 inoperable	Yes	113	Isodose 67%	35	Progression of treated lesion	92% (3 years)	76% (3 years)	Tumor volume (larger GTV)	Age, tumor location	NA	NA	NA	NA
Fakiris (2009) [19]	Non randomized Phase II	70	35/35	70 inoperable	Yes	180–211.2 (195.6)	Isodose 80%	50, 2	Progression of treated lesion	88% (3 years)	87.1% (3 years)	NA	NA				
Timmerman (2010) [36]	Non randomized Phase II	55	44/11	55 inoperable	Yes	151, 2	Isodose 95%	34, 4	Recurrence								
Senthi (2012) [61]	Retrospective	676	379/267	207/459	Yes	105									NA	NA	NA
Taremi (2012)	Prospective										(4 years)	NA	NA	NA	NA	NA	NA
									Progression of treated lesion	93,5% (4 years)	57% (4 years)	NA	NA	NA	Tumor size	Stage	Histology
			52	inoperable	Yes	90–151.2	Isodose 95%	15, 2	Progression of treated lesion	NA	NA	Dose regimen	ECOG, Age, Sex, Tumor diameter or volume (GTV, PTV), T stage	Tumor volume (GTV)	Dose regimen, ECOG, Age, Sex, Tumor diameter or volume (PTV), T stage	ECOG	Dose regimen, Age, Sex, Tumor diameter or volume (GTV, PTV), T stage
Jeppesen (2013) [15]	Retrospective (conventionnal vs SABR)	132	83/49	132 inoperable	Yes	112–211	Isodose 95%	35, 4	Progression of treated lesion	93% vs 89% (1 year) 69% vs 66 % (5 years)	NA	NA	NA	NA	NA	NA	NA
Vanden berg (2015) [60]	Retrospective	197	126/76	NA	Yes	90–180 (149)	Isodose 80%	61	Recurrence in the same lobe	80% (5 years)	65.69% (5 years)	NA	NA	NA	NA	NA	NA
Chang (2015) [6]	Pooled phase III	31	4/27	31 operable	Yes	112.5–151.3	STARS:95% ROSEL:95%	40, 2	Recurrence in the same lobe	96% (3 years)	97% (3 years)	NA	NA	NA	NA	NA	NA
Shibamoto (2015) [7]	Non randomized Phase II	180	128/52	60 operable/120 inoperable	Yes	92.4–119.6 (109.35)	Isocentre	52, 5	Progression of treated lesion	82.6% (5 years)	76.3 (5 years)	None	Age, sex, histology,T stage (1vs2), operability, tumor location, dose	none (T stage: $p = 0.051$)	age, sex, histology,T stage (1vs2), operability, tumor location, dose	None	Age, sex, histology, T stage (1vs2), operability, tumor location, dose
Nagata (2015) [16]	Non randomized phase II	169	169	65 operable/104 inoperable	Yes	105, 6	Isocentre	47 months for inoperable patients 67 months for operable patients	Progression of treated lesion	68,4% (3 years)	NA	NA	NA	NA	NA	NA	NA

M: male, F: female, NA: non available, SCC: squamous cell carcinoma, ADK: adenocarcinoma, LR: local relapse, RR: regional relapse, DR: distant relapse; FU: follow-up, Pred: predictive factors, NS: not significant.

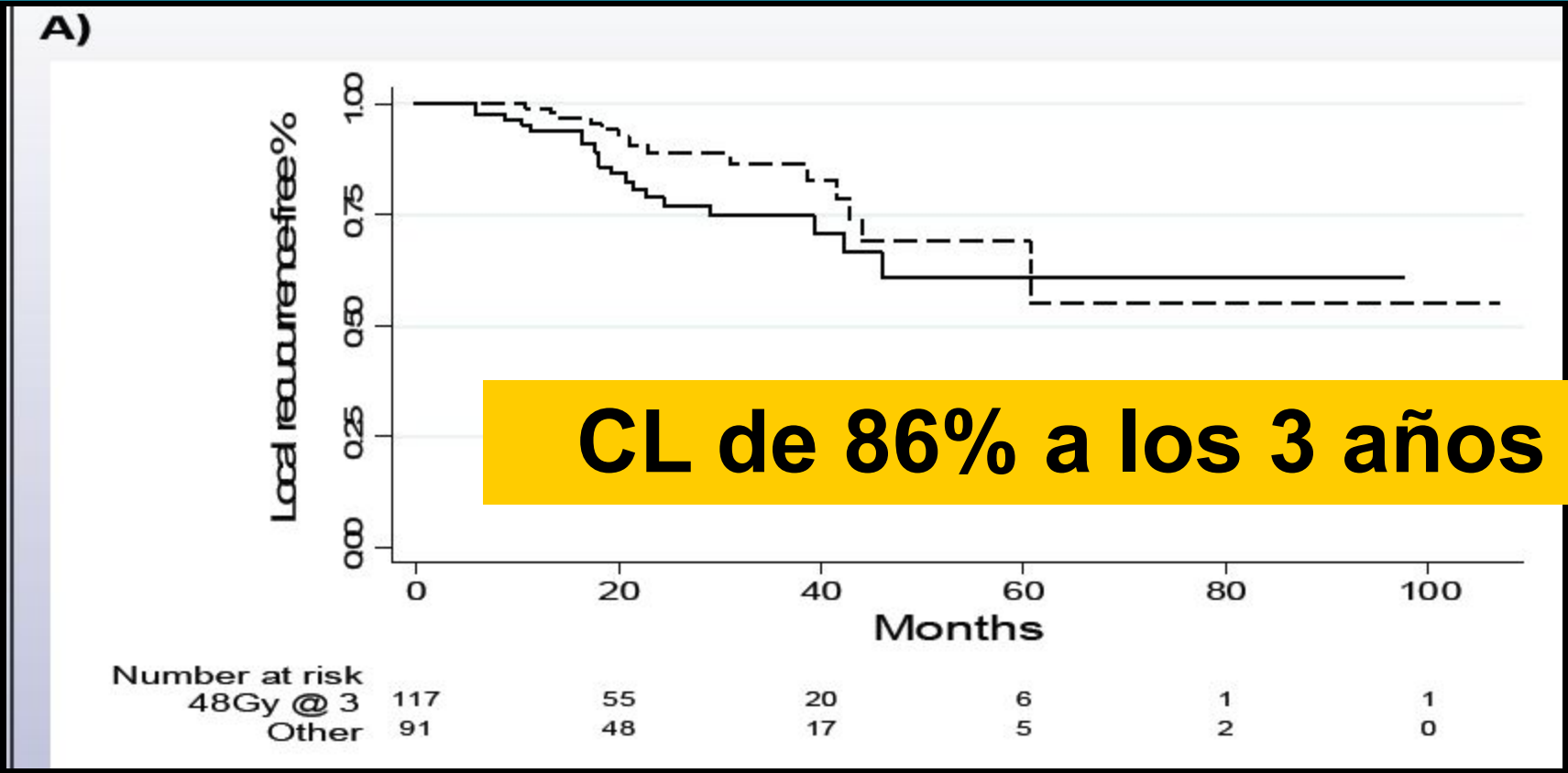
CL de 70% a 96% a los 2-3 años

G. Loganadane et al. / Cancer Treatment Reviews 50 (2016) 240–246

Datos de Mcgill usando 48 Gy en 3 fracciones

Stereotactic Body Radiation Therapy with 48Gy in 3 fractions is an Effective Regimen for Treatment of Peripheral Early Stage Non-Small Cell Lung Cancer

Khaled Adil, Claudie Laprise, Andre Boustead, Issam El Naqa, Marie Duclos, Neil Kopek, Sergio Faria, Bassam Abdulkarim, Hani Al-Halabi *
* Division of Radiation Oncology, Cedar Cancer Center, McGill University Health Center, Montreal, Qc, Canada



CL de 86% a los 3 años

CPCNP de etapa inicial inoperable: SBRT es el standard

STATE OF THE ART: CONCISE REVIEW

Stereotactic Ablative Radiation Therapy for the Treatment of Early-stage Non–Small-Cell Lung Cancer

CEPO Review and Recommendations

Gino Boily, PhD, Édith Filion, MD,† George Rakovich, MD,‡ Neil Kopek, MD,§ Lise Tremblay, MD,‖ Benoit Samson, MD,¶ Stéphanie Goulet, PhD,* Isabelle Roy, MD,# and the Comité de l'évolution des pratiques en oncologie***

Journal of Thoracic Oncology® • Volume 10, Number 6, June 2015

CPCNP de etapa inicial inoperable: SBRT es el standard

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Recommendations: Considering the evidence available to date, the Comité de l'évolution des pratiques en oncologie recommends the following: (1) for medically operable patients with stage T1-2N0M0 NSCLC, surgery remains the standard treatment because comparative data regarding the efficacy of SABR and surgery are currently insufficient for SABR to be considered an equivalent alternative to surgery for these patients; (2) for medically inoperable patients with stage T1-2N0M0 NSCLC or medically operable patients who refuse surgery, SABR should be preferred to standard EBRT (grade B recommendation); (3)

CPCNP de etapa inicial operable: Cirugía versus SBRT

RTOG 1021 Protocol Information

A Randomized Phase III Study of Sublobar Resection (+/- Brachytherapy) versus Stereotactic Body Radiation Therapy in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC)

Protocol Documents

Principal Investigator: Robert Timmerman, MD

Primary Objective:
To ascertain whether patients treated by SBRT have a 3-year overall survival rate that is no more than 10% less than patients treated with sublobar resection

Patient Population:
Patients with biopsy-proven NSCLC who are at high risk for surgery (as specified in the protocol); tumor verified by a thoracic surgeon to be in a location that will permit sublobar resection;

NOTE: Protocol and forms available on CTSU website at www.ctsu.org listed under ACOSOG Z4099

Target Accrual: 420

Current Accrual: 10

Status: Closed to Accrual

Date: 5/15/2013

CPCNP de etapa inicial operable: Cirugía versus SBRT

ClinicalTrials.gov
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Randomized Study to Compare CyberKnife to Surgical Resection In Stage I Non-small Cell Lung Cancer (STARS)

This study has been terminated.
(Lack of enrollment)

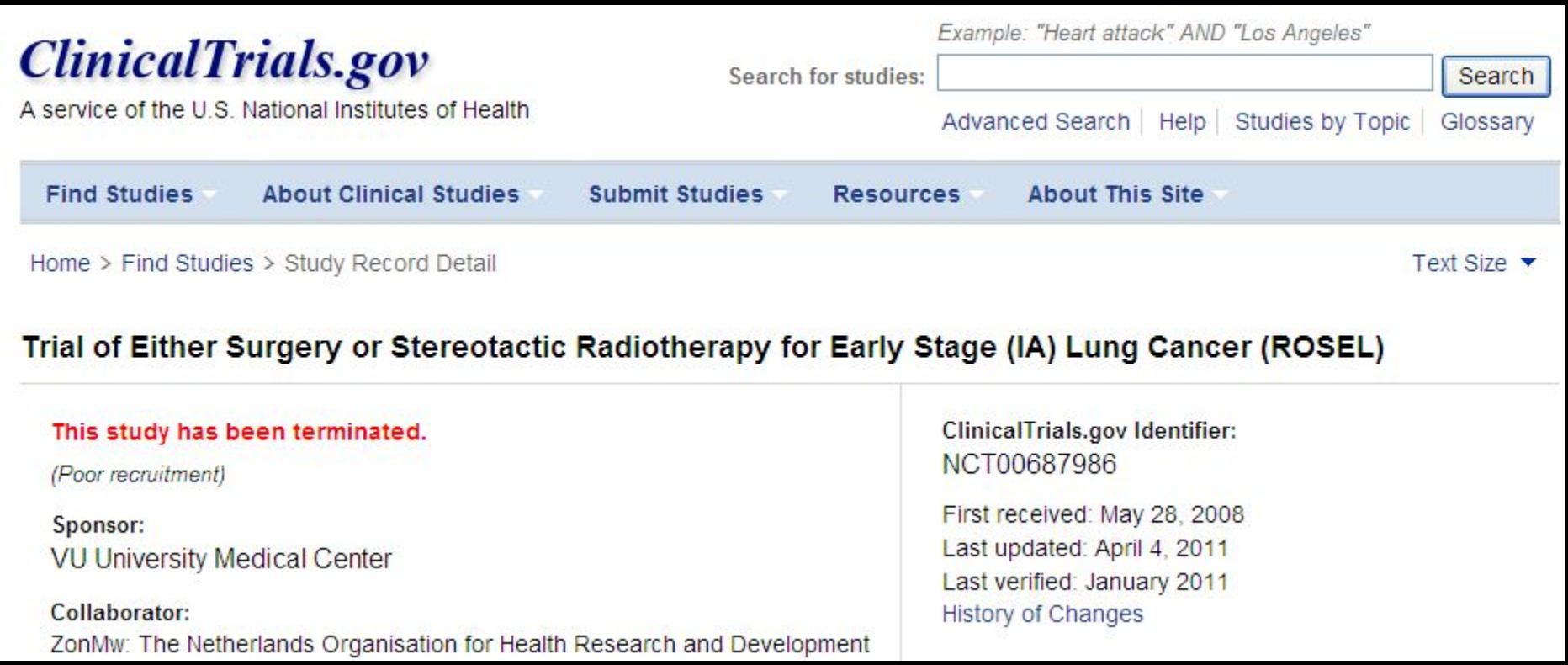
Sponsor:
Accuray Incorporated

Collaborator:

ClinicalTrials.gov Identifier:
NCT00840749

First received: February 7, 2009
Last updated: April 5, 2013
Last verified: April 2013
History of Changes

CPCNP de etapa inicial operable: Cirugía versus SBRT



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Trial of Either Surgery or Stereotactic Radiotherapy for Early Stage (IA) Lung Cancer (ROSEL)

This study has been terminated.

(Poor recruitment)

Sponsor:
VU University Medical Center

Collaborator:
ZonMw: The Netherlands Organisation for Health Research and Development

ClinicalTrials.gov Identifier:
NCT00687986

First received: May 28, 2008
Last updated: April 4, 2011
Last verified: January 2011
History of Changes

CPCNP de etapa inicial operable: Cirugía versus SBRT

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials

Joe Y Chang, Suresh Senan*, Marinus A Paul, Reza J Mehran, Alexander V Louie, Peter Balter, Harry J M Groen, Stephen E McRae, Joachim Widder, Lei Feng, Ben E E M van den Borne, Mark F Munsell, Coen Hurkmans, Donald A Berry, Erik van Werkhoven, John J Kresl, Anne-Marie Dingemans, Omar Dawood, Cornelis J A Haasbeek, Larry S Carpenter, Katrien De Jaeger, Ritsuko Komaki, Ben J Slotman, Egbert F Smit†, Jack A Roth†*

Lancet Oncol 2015; 16: 630–37

Cirugía versus SBRT

Lancet Oncol 2015; 16: 630–37

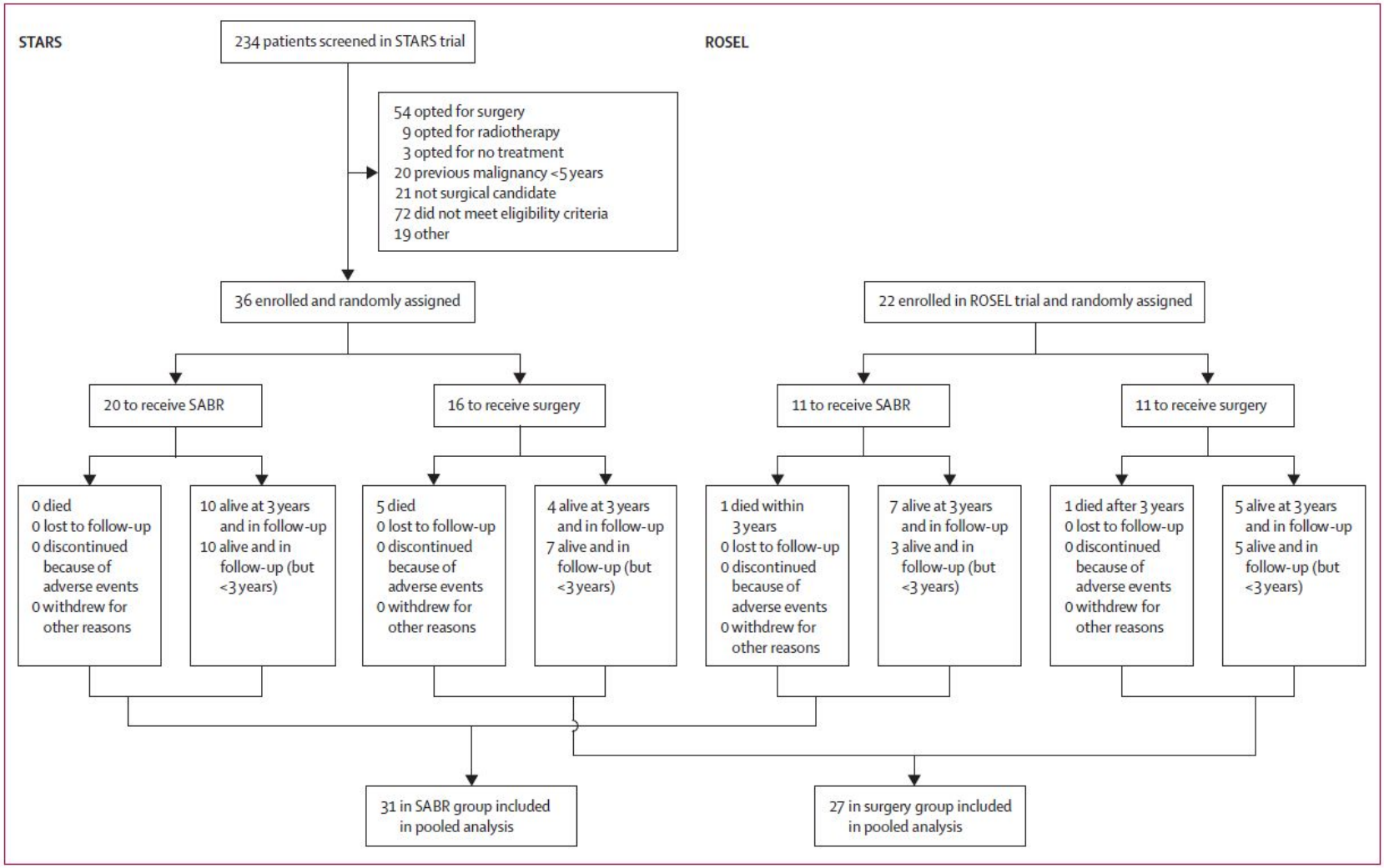


Figure 1: **Study design for STARS and ROSEL trials**
SABR=stereotactic ablative radiotherapy.

Cirugía versus SBRT

Lancet Oncol 2015; 16: 630–37

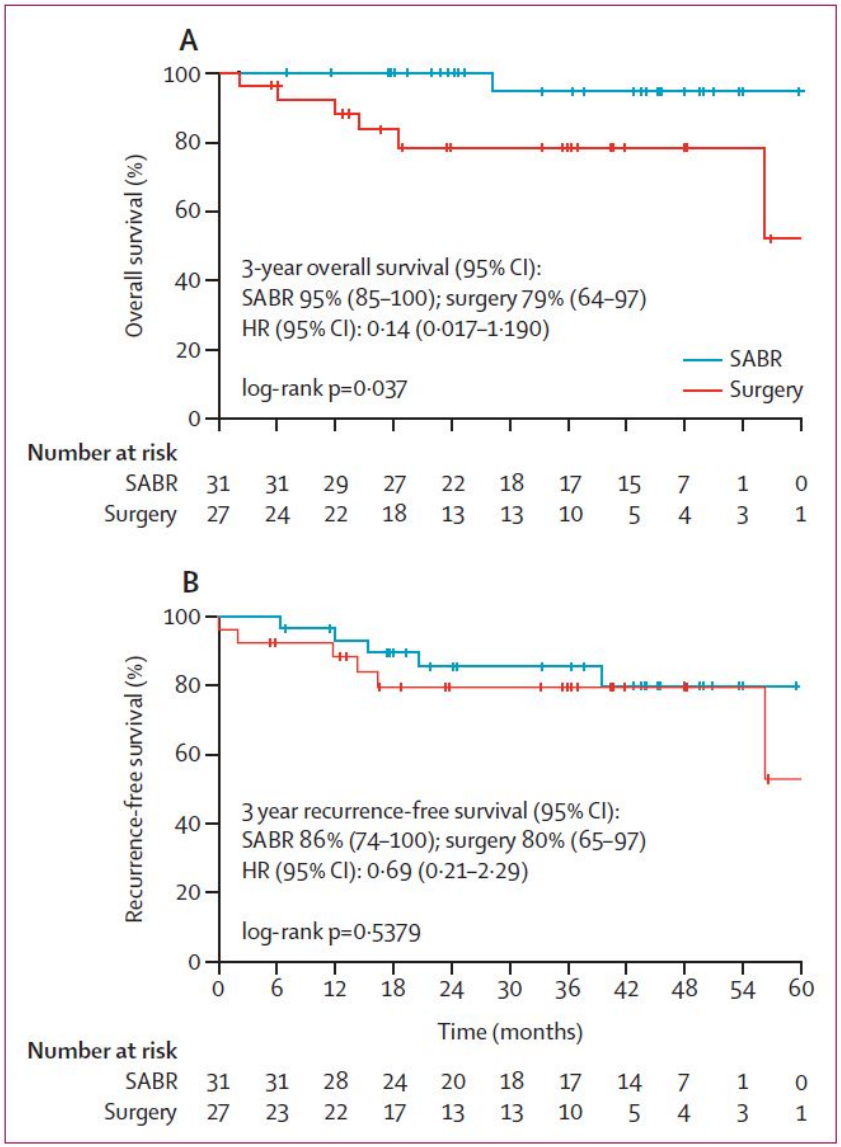


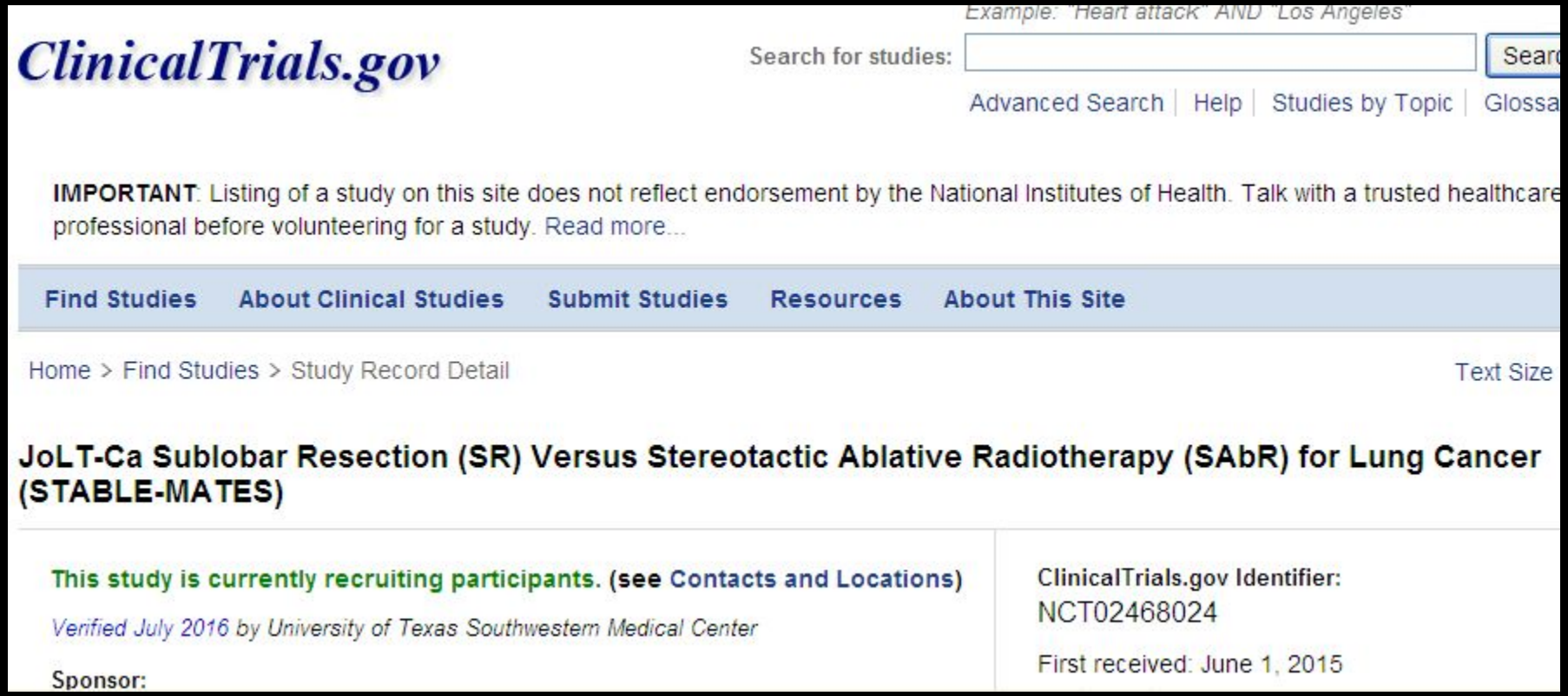
Figure 2: **Overall survival (A) and recurrence-free survival (B)**
One patient died and five had recurrence in the SABR group compared with six and six patients, respectively, in the surgery group. SABR=stereotactic ablative

Cirugía versus SBRT

Lancet Oncol 2015; 16: 630–37

Interpretation SABR could be an option for treating operable stage I NSCLC. Because of the small patient sample size and short follow-up, additional randomised studies comparing SABR with surgery in operable patients are warranted.

Surgery versus SBRT



ClinicalTrials.gov

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Text Size

JoLT-Ca Sublobar Resection (SR) Versus Stereotactic Ablative Radiotherapy (SAbR) for Lung Cancer (STABLE-MATES)

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2016 by University of Texas Southwestern Medical Center

Sponsor:

ClinicalTrials.gov Identifier:
NCT02468024

First received: June 1, 2015

Surgery versus SBRT

Snee *et al. Pilot and Feasibility Studies* (2016) 2:5
DOI 10.1186/s40814-016-0046-2

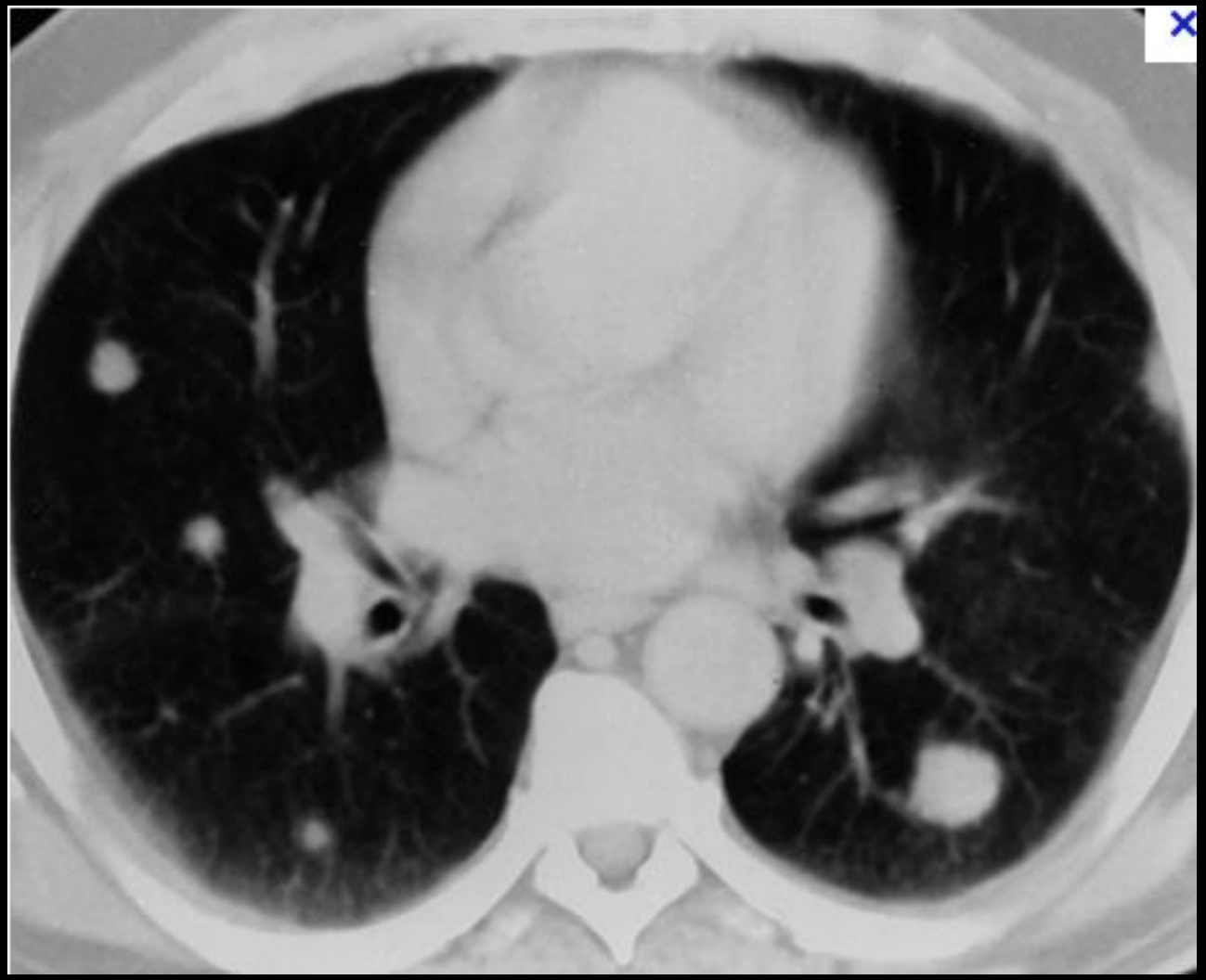
Pilot and Feasibility Studies

STUDY PROTOCOL Open Access

The SABRTooth feasibility trial protocol: a study to determine the feasibility and acceptability of conducting a phase III randomised controlled trial comparing stereotactic ablative radiotherapy (SABR) with surgery in patients with peripheral stage I non-small cell lung cancer (NSCLC) considered to be at higher risk of complications from surgical resection

M. P. Snee[1], L. McParland[2], F. Collinson[2], C. M. Lowe[2], A. Striha[2], D. R. Baldwin[3], B. Naidu[4], D. Sebag-Montefiore[1,6], W. M. Gregory[2], J. Bestall[5], J. Hewison[5], S. Hinsley[2] and K. Franks[1*]

SBRT por las oligometastasas



SBRT gana impulso en el tratamiento de metástasis

ORIGINAL ARTICLE

Definitive Stereotactic Body Radiotherapy (SBRT) for Extracranial Oligometastases

An International Survey of >1000 Radiation Oncologists

American Journal of Clinical Oncology • Volume 00, Number 00, ■■ 2015 www.amjclinicaloncology.com

TABLE 1. Survey Population

Characteristics	Respondents (n [%])	Respondents Using SBRT for OM (%)	Respondents *NOT* Using SBRT for OM (%)
Radiation oncologists	1007 (100)	61.0	39.0
Geographic location			
United States	426 (42)	68.5	31.5
Canada	113 (11)	47.8	52.2
Japan	101 (10)	45.2	54.8
Western Europe	67 (7)	76.1	31.4
Australia/ New Zealand	64 (6)	27.0	73.0
South Korea	26 (3)	78.3	21.3
Miscellaneous			
Practice type			
Academic	421 (42)	66.6	33.4
Private	117 (12)	60.1	39.1
Hospital or stand-alone cancer center	321 (32)	52.8	47.2
Other or unreported	148 (15)	6.8	92.6

OM indicates oligometastases; SBRT, stereotactic body radiotherapy.

SBRT gana impulso en el tratamiento de metástasis

ORIGINAL ARTICLE

Definitive Stereotactic Body Radiotherapy (SBRT) for
Extrac

An International S

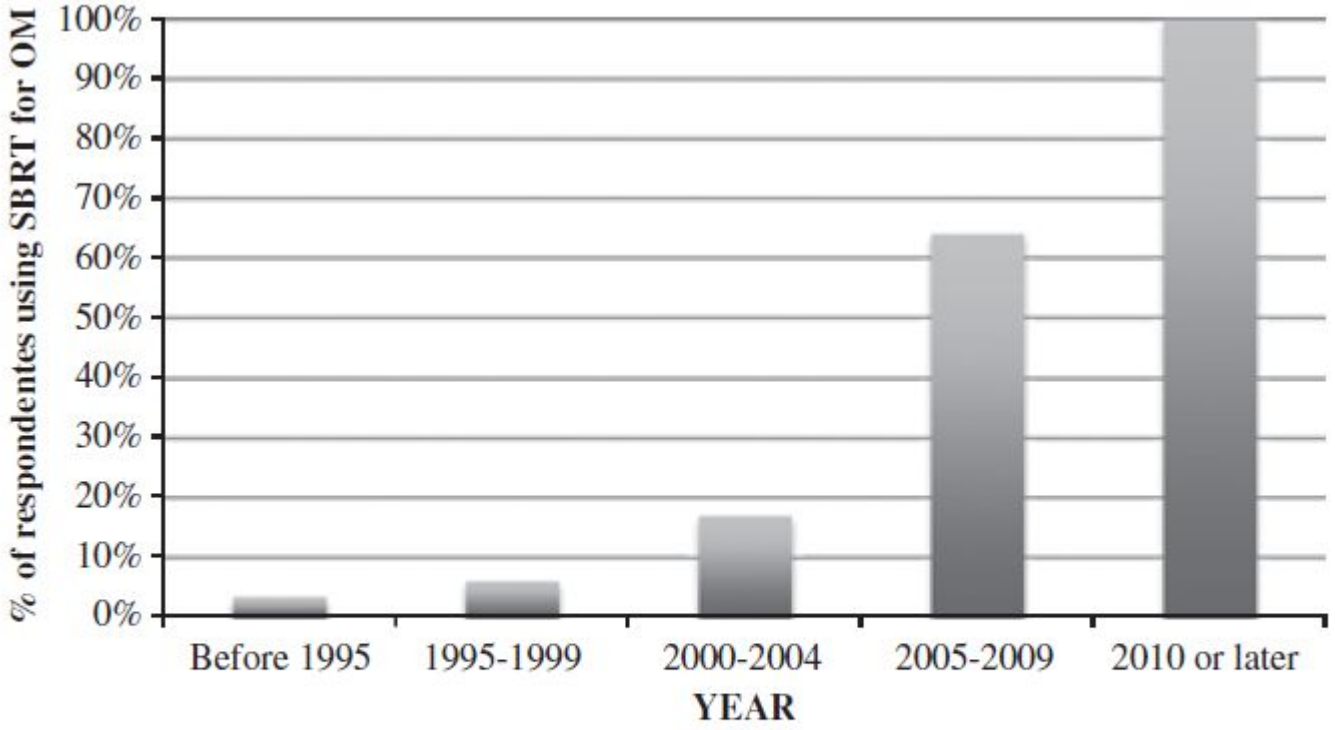


FIGURE 1. Cumulative percentage of respondents using stereotactic body radiotherapy (SBRT) for oligometastases during the defined time intervals.

SBRT gana impulso en el tratamiento de metástasis: Estudios en marcha (prostata)

ClinicalTrials.gov Identifier and Trial Name	Patient Group	Standard Arm	Experimental Arm(s)	Primary End Point	No. of Patients	Estimated Completion Date
Imaging						
NCT00882609	Patients with breast, prostate, or lung cancer undergoing routine bone scans	TC-MDP bone scan	[^{18}F]Fluoride PET/CT	Analysis of diagnostic performance	550	June 2013, status not updated
NCT02680041 (LOCATE)	Patients treated for local prostate cancer with suspicion of recurrent disease	Standard-of-care monitoring	[^{18}F]Fluciclovine PET/CT	Fraction of patients with change in management based on [^{18}F]fluciclovine PET/CT findings	330	December 2018, recruiting
NCT01666808	Prostate adenocarcinoma after prostatectomy with detectable PSA	Standard of care to guide radiation	FACBC PET scan guidance for radiation	Failure-free survival	162	June 2017, recruiting
NCT01815515	Prostate cancer with new or progressive metastatic disease	CT and bone scintigraphy	DCFBC PET	Accuracy of PET/CT detection	25	January 2015
NCT02673151	Increasing PSA after definitive therapy	Bone scan, CT, MRI	^{68}Ga-PSMA PET/CT	Accuracy of ^{68}Ga-PSMA PET/CT	220	June 2021, not yet open
NCT02678351	Patients with intermediate-/high-risk prostate cancer undergoing prostatectomy with lymph node dissection		^{68}Ga-PSMA PET/MRI	Accuracy of ^{68}Ga-PSMA PET/MRI	200	June 2021, recruiting
Surgery						
NCT01407263	Patients with prostate cancer undergoing prostatectomy	Standard lymph node template	Extended lymph node template (vertical *v* horizontal port site closure; 1 *v* 3 days of antibiotic prophylaxis)	Primary: report of hernia; secondary: biochemical recurrence	2,300	July 2021, recruiting
NCT02458716	Newly diagnosed prostate cancer, clinical stage T1-3N1M0 or T1-3N0M1a-b		Surgery followed by standard ADT	Rate of major perioperative complications	50	August 2018, recruiting
Radiation						
NCT02192788	Oligometastatic prostate cancer		SBRT to oligometastases	Number of patients without disease progression	68	August 2019, recruiting
NCT02680587 (ORIOLE)	Oligometastatic prostate cancer	Observation	SBRT to oligometastases	Time to progression	54	March 2021, recruiting

SBRT gana impulso en el tratamiento de metástasis: Estudios en marcha (prostata)

ORIOLE TRIAL: randomized phase II.

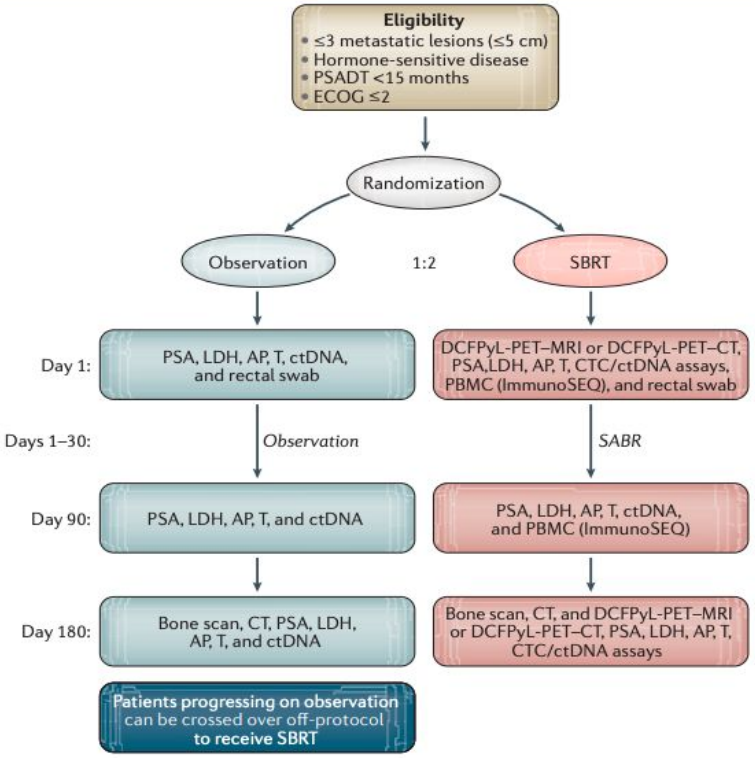


Figure 2 | **Schema for the phase II Randomized Observation versus Stereotactic Ablative Radiation for OLigometastatic Prostate CancEr (ORIOLE) trial.** Men with metachronous hormone-naive oligometastatic disease will be enrolled and dynamically randomized to the schema as shown. AP, alkaline phosphatase; CTCs, circulating tumour cells; ctDNA, cell-free circulating tumour DNA; LDH, lactate dehydrogenase; PBMC, peripheral blood mononuclear cells; SABR, stereotactic ablative radiation; SBRT, stereotactic radiation therapy; T, serum testosterone. ORIOLE is sponsored by the National Cancer Institute (NCI) 1U01CA183031 and a Movember-PCF Challenge Award.

SBRT: buen control local y bien tolerado!

Review

Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Merina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Christopher M Nutting, Peter J Ostler, Nicholas J van As

Lancet Oncol 2013; 14: e28–37

Royal Marsden NHS Foundation Trust, London, UK (A C Tree FRCR, V S Khoo MD, M Ahmed MD, M A Hawkins MD, Prof C M Nutting MD, N J van As FRCR); **Institute of Cancer Research, Sutton, UK** (V S Khoo, Prof D P Dearnaley FRCR, R A Huddart PhD); **Oncogenetics Team, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, London, UK** (Prof R A Eeles FRCR); **and Cancer Centre, Mount Vernon Hospital, Northwood, Middlesex, UK** (P J Ostler FRCR)

Correspondence to:
Dr Alison C Tree, Royal Marsden NHS Foundation Trust, London SW3 6JJ, UK
alison.tree@rmh.nhs.uk

SBRT: buen control local y bien tolerado!

	Study year	Number of patients (number of lesions)	Dose	Primary site	Treated site(s)	Treated metastasis control	Toxicity
Milano et al[53,54]	2008	121 (293)	Various; median 50 Gy in 10 fractions	All (mostly breast and colorectal)	Lung, liver, bone, lymph node, 7 CNS	2-year LLC 77%; 4-year LLC 74%	Grade 3 in 1 patient (1%)
Salama et al[55]	2011	61 (113)	Increasing from 24 Gy in 3 fractions to 48 Gy in 3 fractions	All (26% NSCLC)	Lung, liver, lymph node, bone	2-year LLC 66·7%; 88·0% if dose ≥30 Gy in 3 fractions	Acute grade 3 in 2 (3%), 6 possible late grade 3 (10%)
Kang et al[56]	2010	59 (78)	42 Gy in 3 fractions	Colorectal	Lung, liver, lymph node, other	3-year local control 66% (note 69% of patients had PD after chemotherapy)	No grade 3, 3% grade 4 (gastrointestinal perforation/ obstruction)
							patient); one death (gastric haemorrhage)
Svedman et al[63]	2006	30 (82)	Various: 40 Gy in 4 fractions was most common dose	Renal-cell carcinoma	Lung (majority), renal bed, adrenal	Only 2% documented progression at median follow-up 52 months	4% of side-effects were grade 3
Nuyttens et al[64]	2007	14 (15)	Median 7 Gy/fraction, median 6 fractions	Mixed	Mixed	100% local control at median follow-up 18 months	No grade 3
Greco et al[65]	2011	103 (126)	18–24 Gy in 1 fraction	Prostate, renal, colorectal	Majority bone, lymph node, soft tissue	Local control at 2 years 64% (82% if >22 Gy, 25% for 18–20 Gy)	<4% grade 3 late (stricture, neuritis)

LLC=lesion local control. NSCLC=non-small cell lung cancer. PD=progressive disease.

Table 2: Stereotactic body radiotherapy for mixed oligometastatic sites

CL de 70 a 90% a los 2-3 años

Toxicidad aguda grado 3 o 4 < 5%

www.thelancet.com/oncology Vol 14 January 2013

El objetivo de SBRT en el cáncer metastásico

1. SBRT para la sobrevida a largo plazo: ablation de todos los sitios metastásicos

Ablación versus no ablación: SABRT COMET

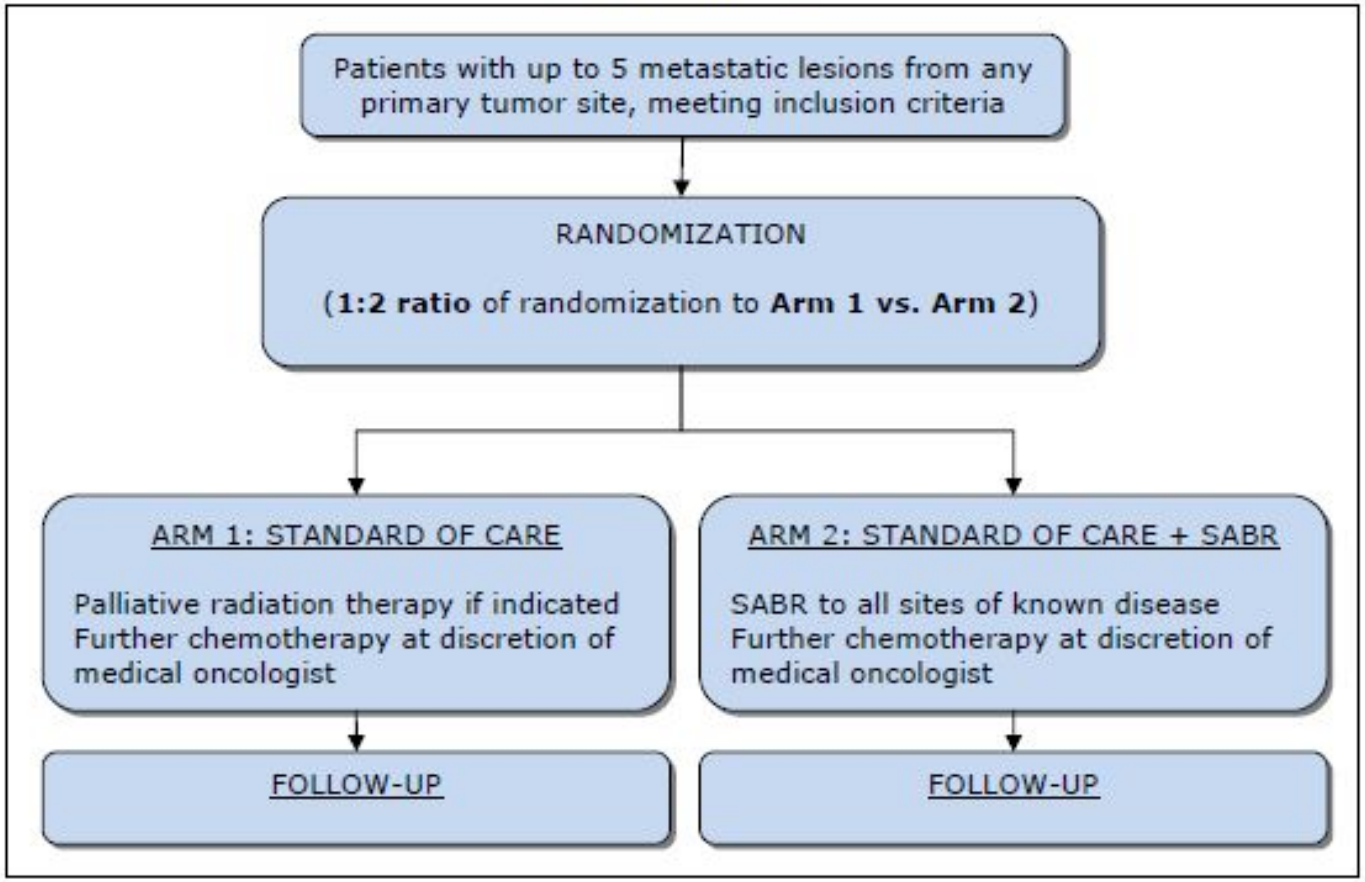
Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial

David A Palma, Robert Olson, Stephen Harrow, Stewart Gaede, Alexander V Louie, Cornelis Haasbeek, Liam Mulroy, Michael Lock, George B Rodrigues, Brian P Yaremko, Devin Schellenberg, Belal Ahmad, Gwendolyn Griffioen, Sashendra Senthi, Anand Swaminath, Neil Kopek, Mitchell Liu, Karen Moore, Suzanne Currie, Glenn S Bauman, Andrew Warner, Suresh Senan

McGill www.thelancet.com **Published online April 11, 2019 http://dx.doi.org/10.1016/S0140-6736(18)32487-5**

Ablación versus no ablación: SABR COMET

STEREOTACTIC ABLATIVE RADIOTHERAPY FOR COMPREHENSIVE TREATMENT OF OLIGOMETASTATIC TUMORS (SABR-COMET): A RANDOMIZED PHASE II TRIAL



McGill www.thelancet.com Published online April 11, 2019 http://dx.doi.org/10.1016/S0140-6736(18)32487-5

Ablación versus no ablación: SABR COMET

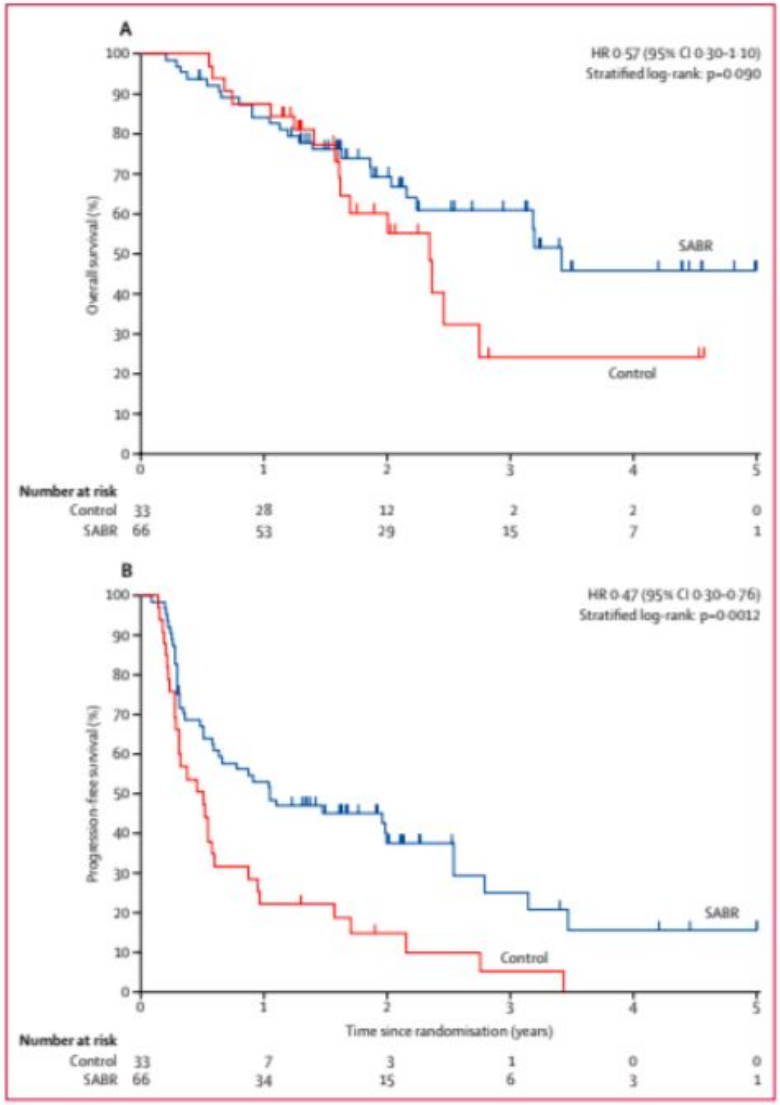


Figure 2: Overall survival (A) and progression-free survival (B)
SABR=stereotactic ablative radiotherapy. HR=hazard ratio.

www.thelancet.com **Published online April 11, 2019** http://dx.doi.org/10.1016/S0140-6736(18)32487-5

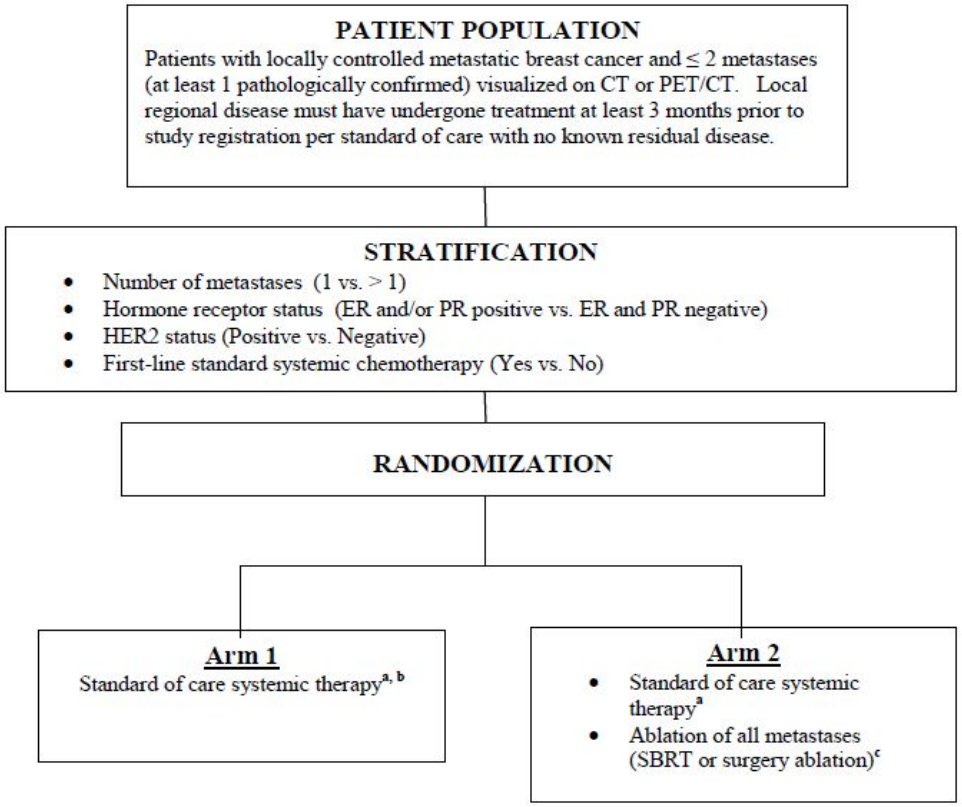
Ablación versus no ablación: ensayos aleatorios en curso

NRG ONCOLOGY

NRG -BR002

A Phase IIR/III Trial of Standard of Care Therapy with or without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer

SCHEMA



Ablación versus no ablación: ensayos aleatorios en curso

RESEARCH UPDATE

Pulmonary metastasectomy in colorectal cancer: the PulMiCC trial

Tom Treasure,[1] Lesley Fallowfield,[2] Belinda Lees,[3] Vern Farewell[4]

Thorax 2012;**67**:185—187. doi:10.1136/thoraxjnl-2011-200015

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Text Size

A Randomized Phase II Study Assessing the Efficacy of Local Consolidative Therapy for Non-Small Cell Lung Cancer Patients With Oligometastatic Disease

This study is currently recruiting participants. (see Contacts and Locations)
Verified August 2015 by M.D. Anderson Cancer Center

Sponsor:
M.D. Anderson Cancer Center

Information provided by (Responsible Party):
M.D. Anderson Cancer Center

ClinicalTrials.gov Identifier:
NCT01725165

First received: November 8, 2012
Last updated: August 6, 2015
Last verified: August 2015
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Tratamiento local de metástasis: estudio aleatorio

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

Daniel R Gomez, George R Blumenschein Jr, J Jack Lee, Mike Hernandez, Rong Ye, D Ross Camidge, Robert C Doebele, Ferdinandos Skoulidis, Laurie E Gaspar, Don L Gibbons, Jose A Karam, Brian D Kavanagh, Chad Tang, Ritsuko Komaki, Alexander V Louie, David A Palma, Anne S Tsao, Boris Sepesi, William N William, Jianjun Zhang, Qiuling Shi, Xin Shelley Wang, Stephen G Swisher, John V Heymach**

Lancet Oncol 2016; 17: 1672–82

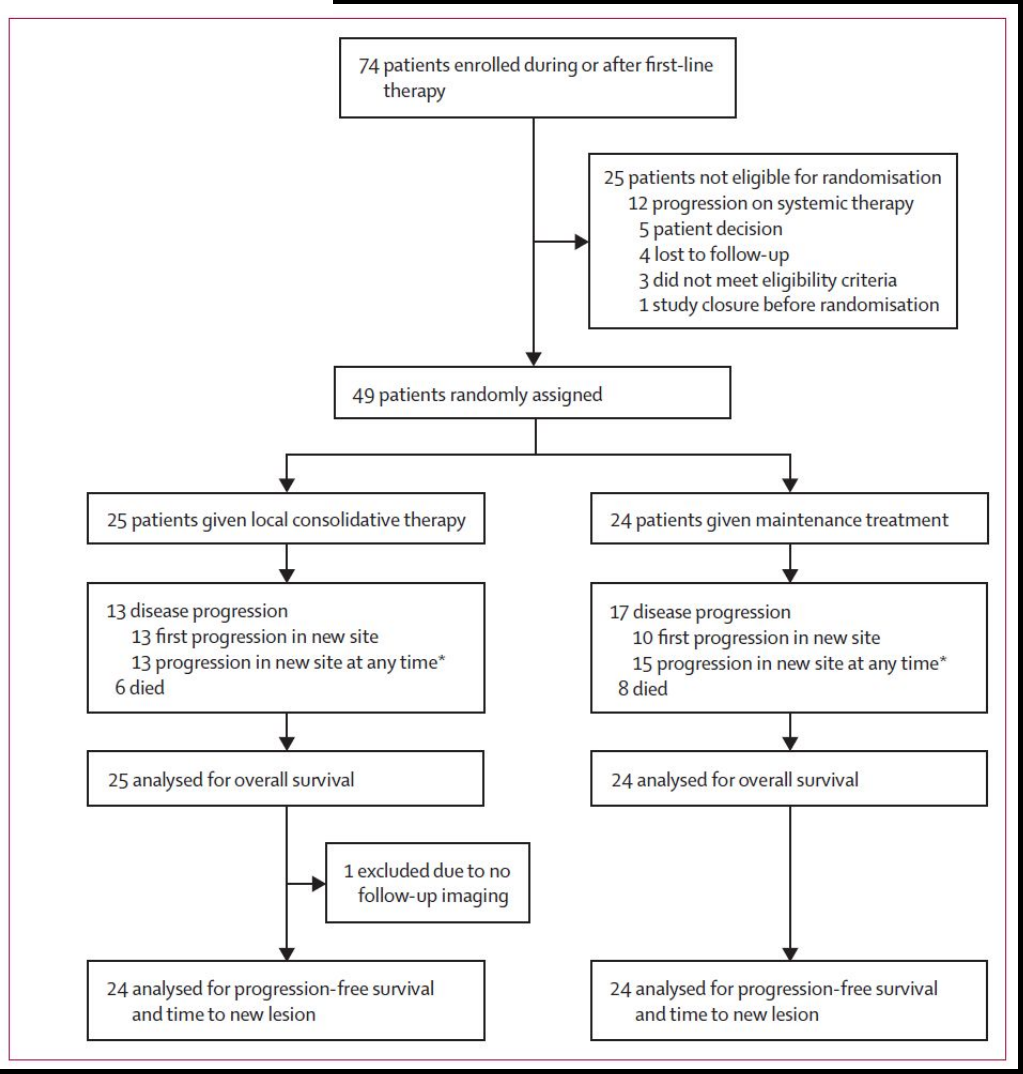
Procedures

Patients who were randomly allocated to the local consolidative therapy group were treated with the intent to ablate all residual disease (primary tumour, lymph nodes, and metastatic sites as appropriate) with surgery, radiotherapy, or both. The type of local consolidative therapy was determined in consultation with multidisciplinary teams. The choice of dose-fractionation regimen was made by the treating radiotherapist, with curative intent when possible. Stereotactic ablative body radiotherapy, intermediate hypofractionated radiotherapy (eg, 15 fractions to the mediastinum), and concurrent chemoradiotherapy were allowed.

Tratamiento local de metástasis: estudio aleatorio

Lancet Oncol 2016; 17: 1672–82

Terminado temprano después del análisis intermedio planificado después de 44 eventos.



Tratamiento local de metástasis: estudio aleatorio

Lancet Oncol 2016; 17: 1672–82

Sobrevida libre de recurrencia media:

Tratamiento local de metástasis: 11.9 meses
Sin tratamiento local de metástasis: 3.9 meses

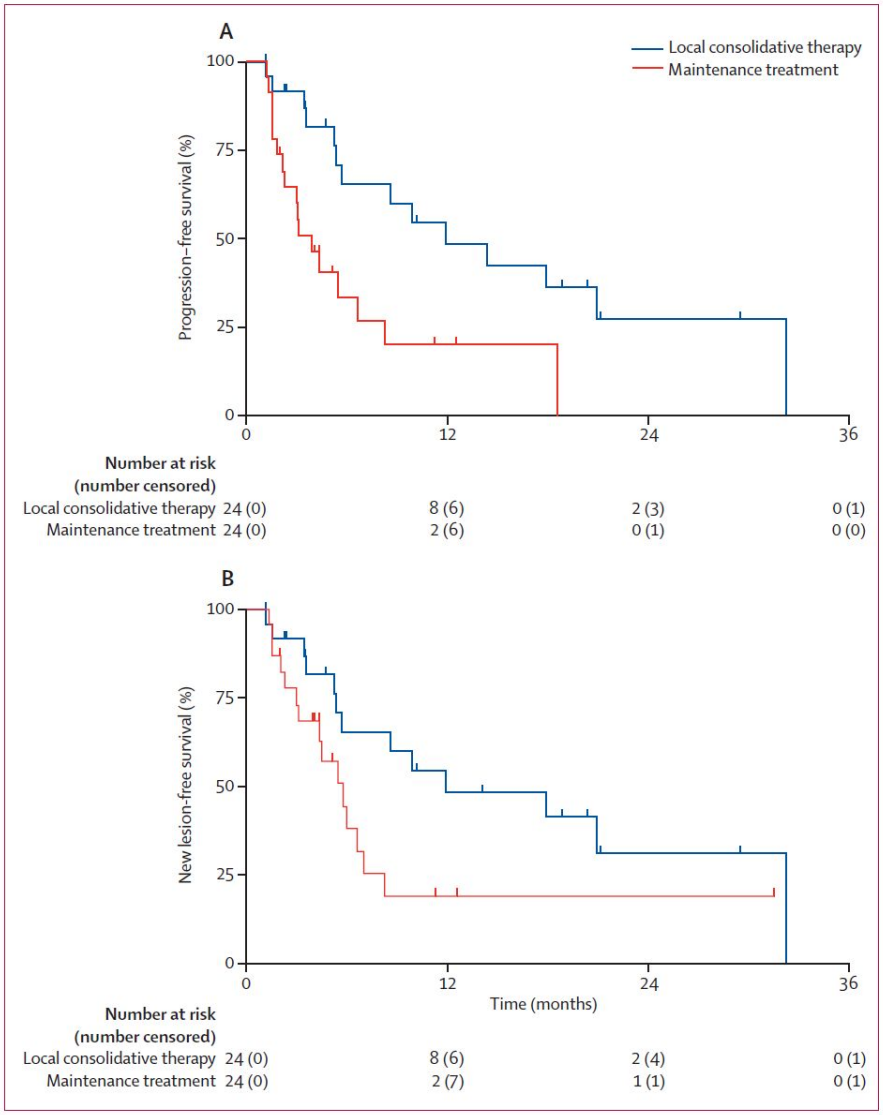


Figure 2: Progression-free survival (A) and time to appearance of disease at a new site (B)

Mientras tanto…..

Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Merina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Christopher M Nutting, Peter J Ostler, Nicholas J van As

www.thelancet.com/oncology Vol 14 January 2013

Panel: Evidence-based practice for extracranial oligometastases

- Stereotactic body radiotherapy results in a high control rate of treated metastases (~80%)
- About 20% of patients are progression free at 2–3 years after stereotactic body radiotherapy
- Toxicity is low
- Stereotactic body radiotherapy should be considered in patients with isolated metastases, especially if the disease-free interval is longer than 6 months
- Randomised trials are needed to establish whether stereotactic body radiotherapy improves progression free and/or overall survival
- Patients most likely to benefit from stereotactic body radiotherapy have:
  - Long disease-free interval
  - Breast histology
  - One to three metastases
  - Small metastases
  - Higher radiation dose delivered (biologic effective dose >100 Gy)

Mientras tanto…..

Radiotherapy and Oncology 114 (2015) 155–160

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

SBRT of oligometastases

Survival and prognostic factors in 321 patients treated with stereotactic body radiotherapy for oligo-metastases

Mette Marie Fode *, Morten Høyer *

Department of Oncology, Aarhus University Hospital, Denmark

A B S T R A C T

Background and purpose: To establish a model to predict survival after SBRT for oligo-metastases in patients considered ineligible for surgical resection (SR) and radiofrequency ablation (RFA).

Material and methods: Overall survival (OS) rates were estimated in 321 patients treated for 587 metastases with SBRT over 13 years. Patients were treated for a variety of metastasis types with colorectal cancer (CRC) being the most frequent ($n = 201$).

Results: With a median follow-up time of 5.0 years, the median OS was 2.4 years (95% CI 2.3–2.7) and the survival rates were 80%, 39%, 23% and 12% at 1, 3, 5 and 7.5 years after SBRT, respectively. WHO performance status (PS) (0–1) (HR 0.49; $p < 0.001$), solitary metastasis (HR 0.75; $p = 0.049$), metastasis $\leqslant$30 mm (HR 0.53; $p < 0.001$), metachronous metastases (HR 0.71; $p = 0.02$) and pre-SBRT chemotherapy (HR 0.59; $p < 0.001$) were independently related to favorable OS. Median OS rates were 7.5, 2.8, 2.5, 1.7 and 0.8 years with 0, 1, 2, 3, $\geqslant$4 unfavorable prognostic factors, respectively. The treatment-related morbidity was moderate. However, three deaths were possibly treatment-related.

Conclusion: Prognostic factors may predict long-term survival in patients with oligo-metastases treated with SBRT.

 Radiotherapy and Oncology 114 (2015) 155–160

In Mientras tanto…..

ELSEVIER

SBRT of oligon

Survival a
body radic

Mette Marie

Department of Oncolo

Table 3
Multivariate analysis of survival of the total cohort.

Covariate	HR (95% CI)	*p*-Value
Performance status		
0–1	0.49 (0.32–0.74)	<0.001
2–3		
Number of metastasis		
1	0.75 (0.57–0.99)	0.049
2–6		
Size of largest metastasis		
⩽30 mm	0.53 (0.40–0.69)	<0.001
>30 mm		
Timing of metastasis		
Synchronous	0.71 (0.54–0.95)	0.02
Metachronous		
Pre-SBRT chemotherapy		
Yes	0.59 (0.44–0.78)	<0.001
No		

Mientras tanto…..

Radiotherapy and Oncology 114 (2015) 155–160

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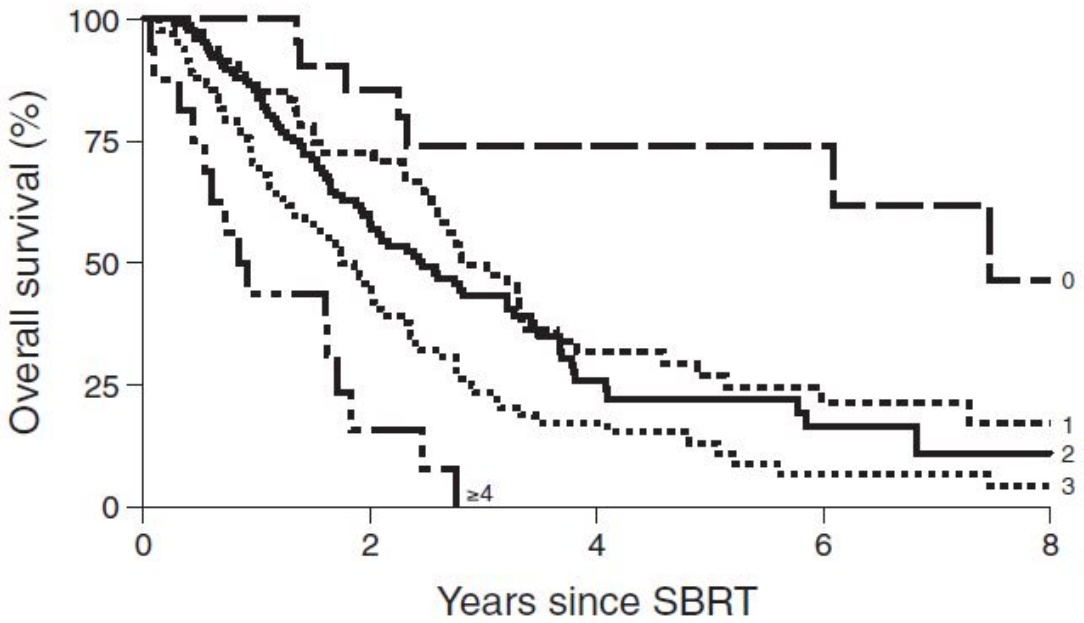
SBRT of oligometastases

Survival and prognostic factors ir
body radiotherapy for oligo-meta

Mette Marie Fode *, Morten Høyer *

Department of Oncology, Aarhus University Hospital, Denmark



No. at risk

0	25	17	10	6	3
1	70	41	14	7	2
2	126	57	15	5	1
3	82	33	10	3	2
≥4	16	2	0	0	0

Fig. 2. Survival by number of unfavorable prognostic factors: performance status, number of metastases, size of the largest metastasis, timing of metastasis and prior chemotherapy.

Predicting the OS benefit from SBRT

Radiotherapy and Oncology 127 (2018) 493–500

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Oligometastases

Comparison of survival and prognostic factors in patients treated with stereotactic body radiotherapy for oligometastases or oligoprogression

Catherine A. Pembroke [a,1,*], Bernard Fortin [b], Neil Kopek [c]

[a] Velindre Cancer Centre, Cardiff, United Kingdom; [b] Department of Radiation Oncology, Hôpital Maisonneuve-Rosemont; and [c] Department of Radiation Oncology, McGill University Health Centre, Montreal, Canada

ARTICLE INFO

Article history:
Received 15 January 2018
Received in revised form 17 April 2018
Accepted 18 April 2018
Available online 4 May 2018

Keywords:
Oligoprogression
Oligometastases
Stereotactic radiotherapy
SBRT

ABSTRACT

Background and purpose: Clinical ch
support the use of ablative strategi
ing stereotactic body radiotherapy
Material and methods: Overall (OS)
for 209 lesions (106 OM and 57
calculated using the Kaplan–Meier
and cumulative incidences of loca
respectively.
Results: The median OS and PFS w
groups respectively ($P = 0.02$ and P
(1/2 vs ⩾3 HR 1.88) were indepe
versus 22%/6% in the OM and OP
irradiated field and OP status (p =
($p = 0.001$) conferred a greater risk
OP groups ($P = 0.001$).
Conclusion: Survival and distant re
static disease and performance sta
with systemic therapies to allow d

Table 4
Multivariate survival analyses by Cox Regression.

	Multivariate HR for OS (95% C.I.)	Multivariate HR for PFS (95% C.I.)
Performance status 2–3 vs 0–1	2.95 (1.60–5.43) $p = 0.0005$	2.11 (1.19–3.73) $p = 0.0107$
Number of metastatic sites 3+ vs 1–2	1.89 (1.21–2.95) $p = 0.0052$	2.93 (1.98–4.33) $p < 0.0001$
Gross tumour volume > 10 cc vs <=10 cc	n.s.	2.43 (1.65–3.57) $p < 0.0001$

OS = overall survival, PFS = progression free survival, C.I = confidence interval, n.s.: not significant.

2. SBRT para control local: ablación de sitios seleccionados

SBRT para oligoprogresión

In the setting of multiple sites of metastatic disease where only a few lesions show progression ie. oligoprogression, SBRT may be considered in an effort to regain control at those sites. This is a common strategy to defer systemic treatment or to avoid abandoning a systemic agent that appears to be globally providing good control of disease at all other sites. In some cases focal treatment of one or a few sites of disease may lead to unexpectedly good response at other distant sites that were not targeted.....

SBRT para oligoprogresión

En el contexto de múltiples sitios de metástasis donde solo unas pocas lesiones muestran progresión, es decir oligoprogresión, SBRT puede considerarse por recuperar el control en esos sitios. Esta es una estrategia común para diferir el tratamiento sistémico o para evitar abandonar un agente sistémico que parece proporcionar un buen control global en todos los otro sitios. En algunos casos, el tratamiento focal de uno o unos pocos sitios de puede conducir a una respuesta inesperadamente buena en otros sitios distantes que no fueron atacados ...

Efecto abscopal

The NEW ENGLAND JOURNAL of MEDICINE

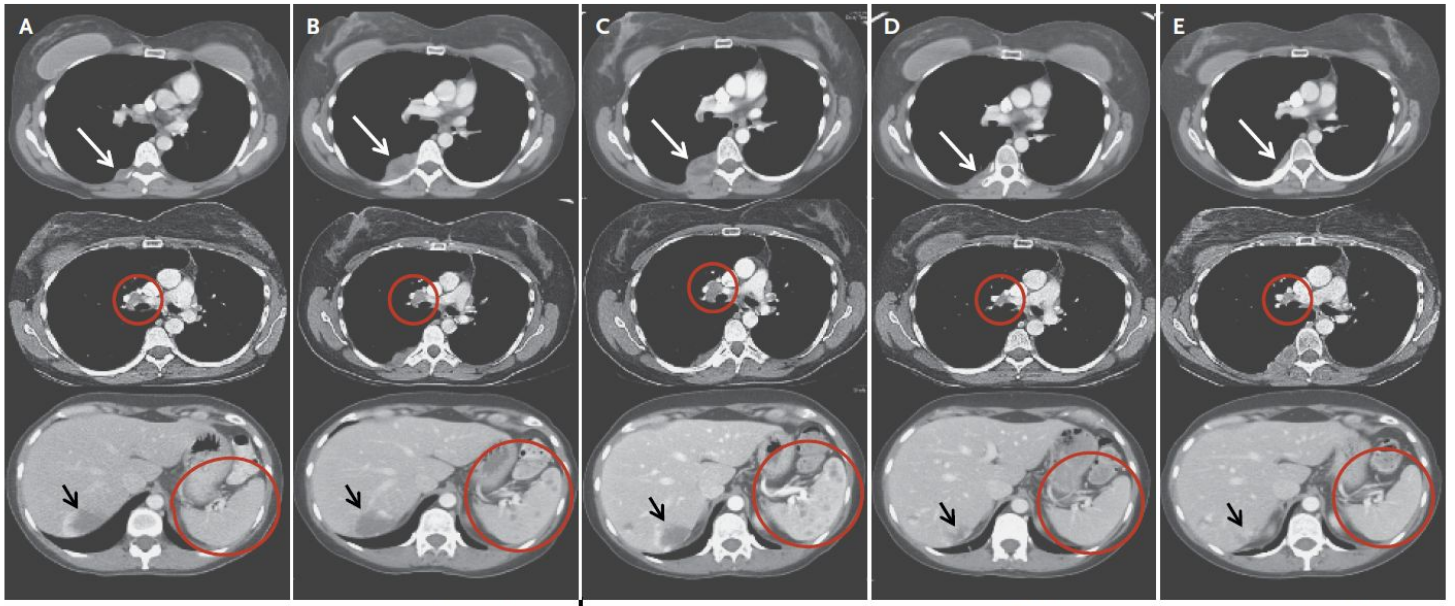
BRIEF REPORT

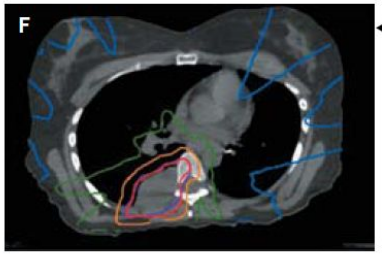
Immunologic Correlates of the Abscopal Effect in a Patient with Melanoma

Michael A. Postow, M.D., Margaret K. Callahan, M.D., Ph.D., Christopher A. Barker, M.D., Yoshiya Yamada, M.D., Jianda Yuan, M.D., Ph.D., Shigehisa Kitano, M.D., Ph.D., Zhenyu Mu, M.D., Teresa Rasalan, B.S., Matthew Adamow, B.S., Erika Ritter, B.S., Christine Sedrak, B.S., Achim A. Jungbluth, M.D., Ramon Chua, B.S., Arvin S. Yang, M.D., Ph.D., Ruth-Ann Roman, R.N., Samuel Rosner, Brenna Benson, James P. Allison, Ph.D., Alexander M. Lesokhin, M.D., Sacha Gnjatic, Ph.D., and Jedd D. Wolchok, M.D., Ph.D.

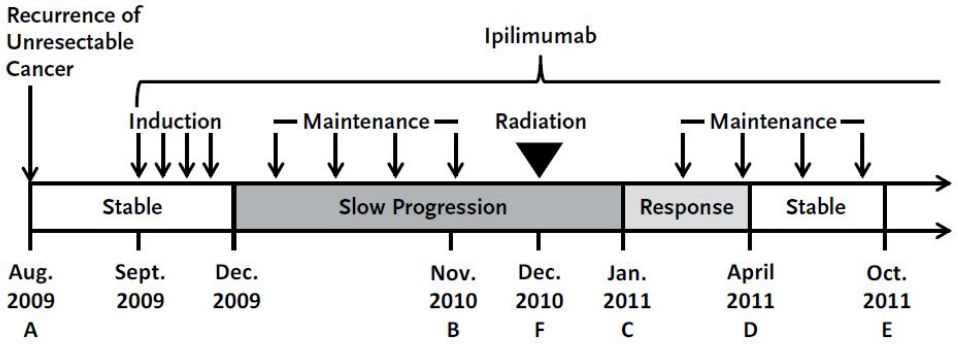
N Engl J Med 2012;366:925-31.

Efecto abscopal: Un ejemplo





December 2010



Efecto abscopal: ¿como funciona?

frontiers in ONCOLOGY

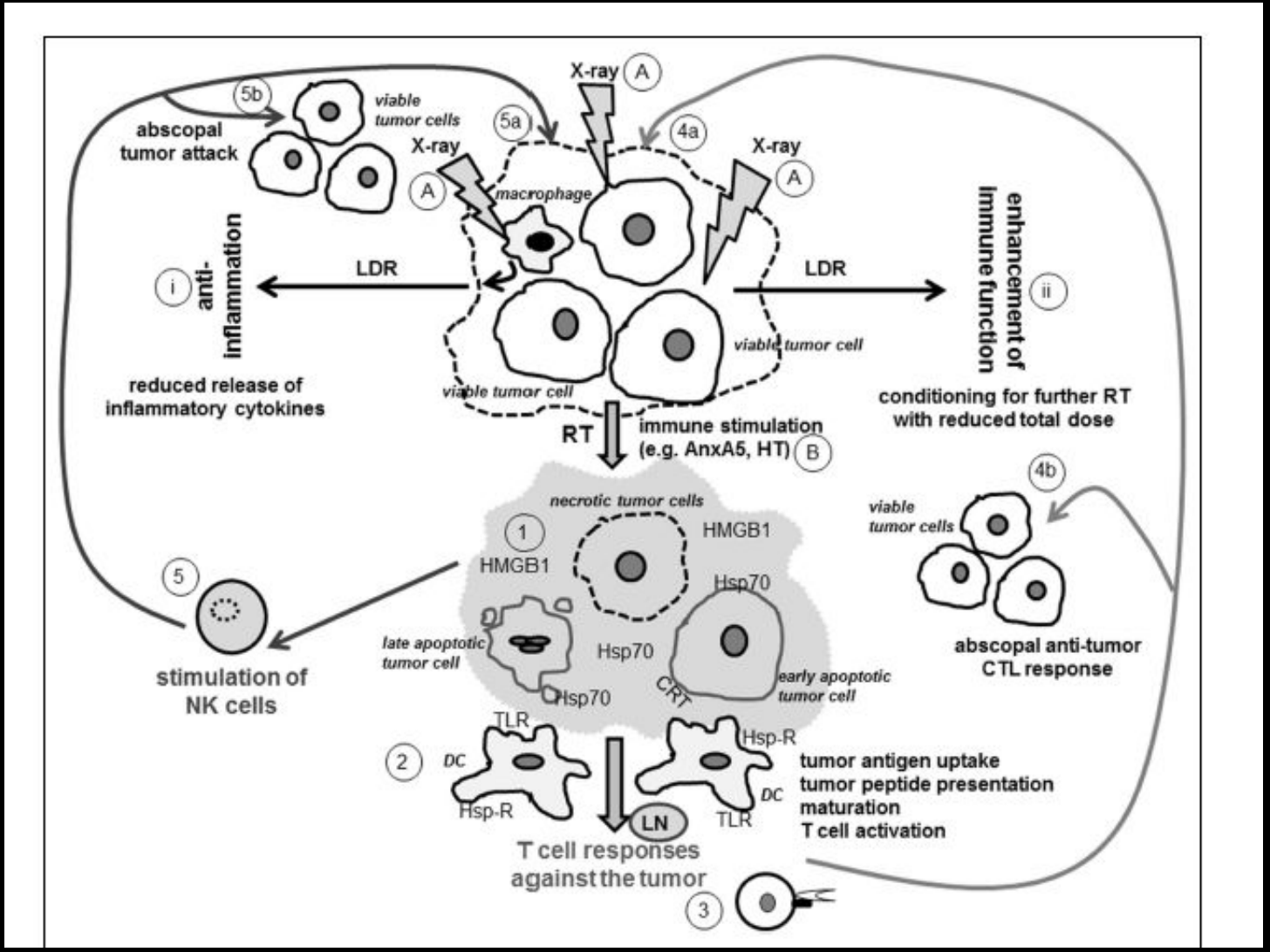
REVIEW ARTICLE
published: 25 July 2012
doi: 10.3389/fonc.2012.00075

How does ionizing irradiation contribute to the induction of anti-tumor immunity?

Yvonne Rubner[1†], Roland Wunderlich[1†], Paul-Friedrich Rühle[1], Lorenz Kulzer[1], Nina Werthmöller[1], Benjamin Frey[1], Eva-Maria Weiss[1], Ludwig Keilholz[2], Rainer Fietkau[1] and Udo S. Gaipl[1]*

[1] *Radiation Immunobiology, Department of Radiation Oncology, University Hospital Erlangen, Friedrich-Alexander Universität Erlangen-Nürnberg, Erlangen, Germany*
[2] *Department of Radiotherapy, Clinical Center Bayreuth, Bayreuth, Germany*

Efecto abscopal: ¿como funciona?



Efecto abscopal: Estudios en curso

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Concurrent Ipilimumab and Stereotactic Ablative Radiation Therapy (SART) for Oligometastatic But Unresectable Melanoma

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2015 by Comprehensive Cancer Centers of Nevada

Sponsor:
Wolfram Samlowski

Collaborator:
Comprehensive Cancer Centers of Nevada

Information provided by (Responsible Party):
Wolfram Samlowski, Comprehensive Cancer Centers of Nevada

ClinicalTrials.gov Identifier:
NCT01565837

First received: March 26, 2012
Last updated: July 18, 2015
Last verified: July 2015
History of Changes

Study Rationale:

Ipilimumab may markedly enhance the immunologic responses to tumor antigen released from necrotic tumor cells by radiotherapy by promoting cytotoxic T cell activation, while preventing induction of antigen tolerance. In addition, further beneficial immunologic effect may be achieved by the reduction in the amount of viable tumor cell mass. The net effect may be to promote a significantly enhanced antitumor T cell response. This will result in improved 1-year and 2-year survival, especially if a minimal or microscopic disease state can be achieved within a patient following SART.

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Trial record **12 of 604** for: SBRT
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A Proof of Principle Study of Pembrolizumab With SBRT in TKI mRCC Patients (OZM-065)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified November 2015 by Sunnybrook Health Sciences Centre

Sponsor:
Sunnybrook Health Sciences Centre

Collaborators:
Merck Sharp & Dohme Corp.
Ozmosis Research Inc.

Information provided by (Responsible Party):
Sunnybrook Health Sciences Centre

ClinicalTrials.gov Identifier:
NCT02599779

First received: September 9, 2015
Last updated: November 5, 2015
Last verified: November 2015
History of Changes

Gracias. ¿Preguntas?