



ΚΑΡΚΙΝΟΣ ΠΝΕΥΜΟΝΑ

ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ

**Γ.Ι. ΠΙΣΣΑΚΑΣ
ΝΟΣ. ΑΛΕΞΑΝΔΡΑ**

ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ



ΠΟΛΥ ΔΕΛΕΑΣΤΙΚΗ ΚΑΙ «ΜΥΣΤΗΡΙΩΔΗΣ» ΜΕΘΟΔΟΣ

ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ



ΑΚΤΙΝΟΘΕΡΑΠΕΥΤΙΚΗ ΜΕΘΟΔΟΣ ΕΞΑΙΡΕΤΙΚΗΣ ΑΚΡΙΒΕΙΑΣ

ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ

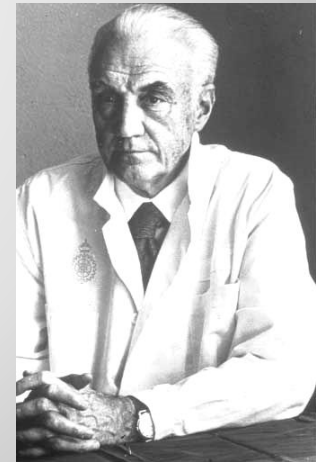
- ΕΡΩΤΗΜΑΤΑ
- ΤΙ ΕΙΝΑΙ;



ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ (γ- knife)

**«ΚΑΤΑΣΤΡΟΦΗ ΕΝΟΣ ΚΑΘΟΡΙΣΜΕΝΟΥ ΜΕ
ΣΤΕΡΕΟΤΑΚΤΙΚΕΣ ΣΥΝΤΕΤΑΓΜΕΝΕΣ
ΕΝΔΟΚΡΑΝΙΑΚΟΥ ΣΤΟΧΟΥ
ΜΕ ΕΦ'ΑΠΑΞ ΧΟΡΗΓΗΣΗ
ΥΨΗΛΗΣ ΔΟΣΗΣ RT ,
ΑΦΗΝΟΝΤΑΣ ΑΘΙΚΤΟ ΤΟ ΚΡΑΝΙΟ»**

LEKSELL 1951



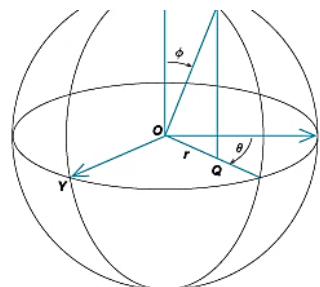
ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ (γ- knife)

ΝΕΥΡΟΧΕΙΡΟΥΡΓΙΚΗ
+
ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

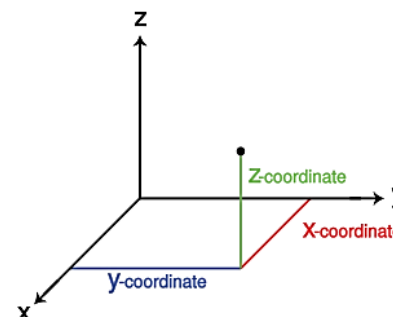
Ο προς ακτινοβολήση όγκος
καθορίζεται με στερεοτακτικά
δεδομένα έξω από το κρανίο

Στερεοταξία:

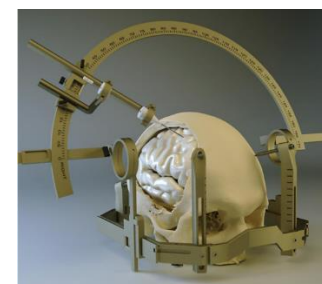
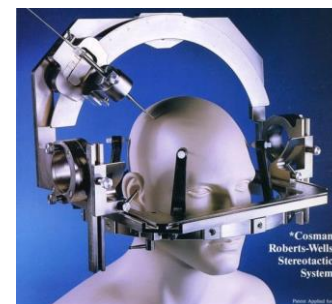
είναι ο προσδιορισμός ενός σημείου
στο χώρο βάσει των αξόνων X, Y, Z
(Καρτεσιανές συντεταγμένες)



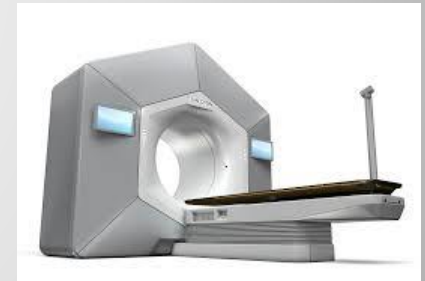
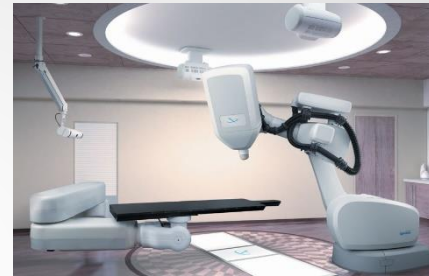
Σύστημα Συντεταγμένων



Σύστημα Συντεταγμένων



Εξέλιξη της τεχνολογίας



Εξέλιξη της τεχνολογίας



Physica Medica
Volume 47, March 2018, Pages 129-138



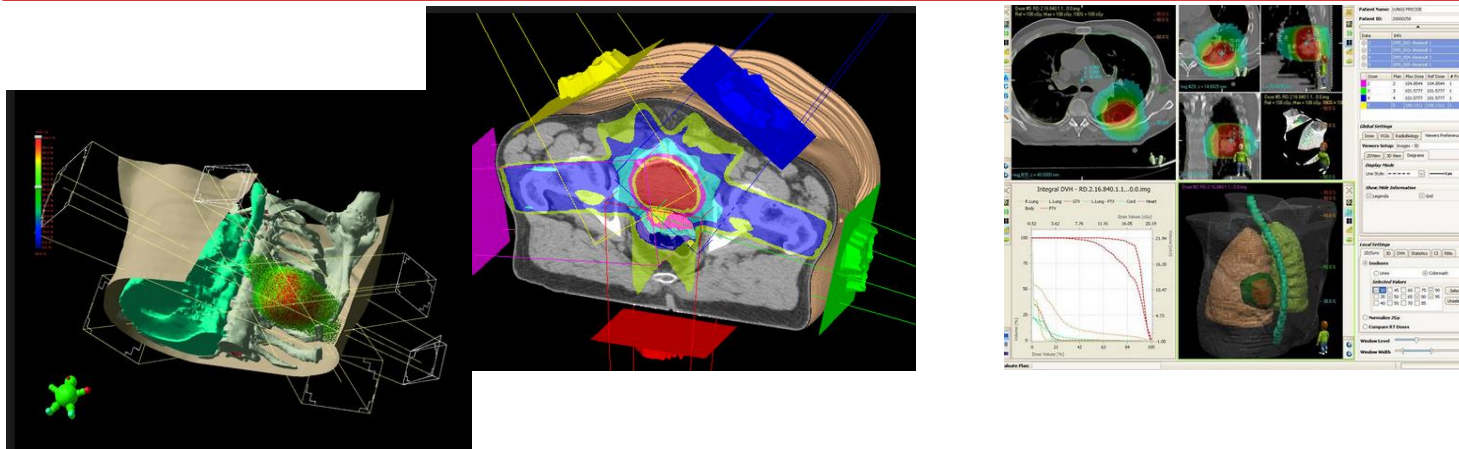
Review paper

The impact of technology on the changing practice of lung SBRT

Marianne Camille Aznar ^{a, b, c}✉, Samantha Warren ^d, Mischa Hoogeman ^e, Mirjana Josipovic ^{e, f}

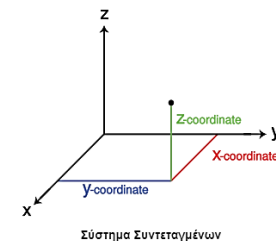
....ΑΛΛΑΞΕ ΟΛΗ ΤΗΝ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

ΣΤΕΡΕΟΤΑΞΙΑ: είναι ο προσδιορισμός ενός σημείου στο χώρο βάσει των αξόνων X, Y, Z
(Καρτεσιανές συντεταγμένες)



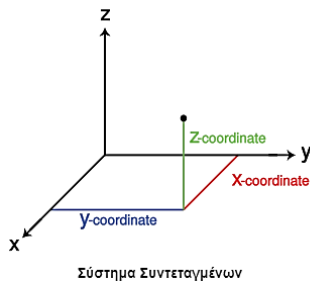
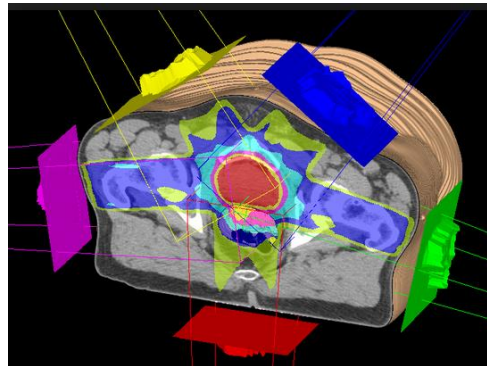
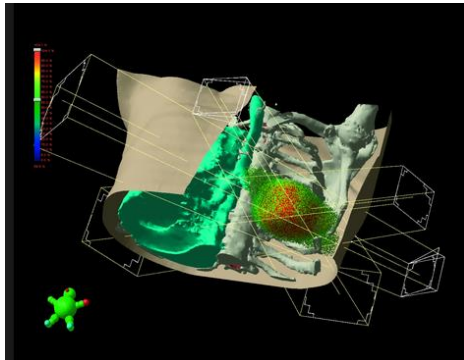
ΟΛΗ Η ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

**ΔΕΝ ΕΧΕΙ ΑΝΑΓΚΗ ΠΙΑ
ΑΠΟ ΤΙΣ ΚΑΡΤΕΣΙΑΝΕΣ ΣΥΝΤΕΤΑΓΜΕΝΕΣ
ΓΙΑ ΝΑ ΒΡΕΙ ΜΕ ΑΠΟΛΥΤΗ ΑΚΡΙΒΕΙΑ ΤΟΝ ΣΤΟΧΟ ΤΗΣ!!!**

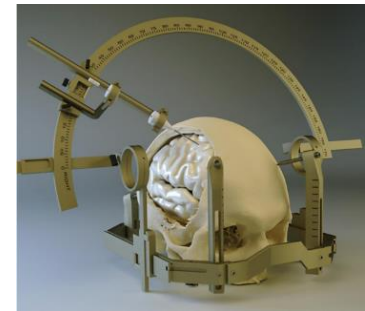


ΣΤΕΡΕΟΤΑΞΙΑ:

είναι ο προσδιορισμός ενός σημείου στο χώρο βάσει των αξόνων X, Y, Z
(Καρτεσιανές συντεταγμένες)

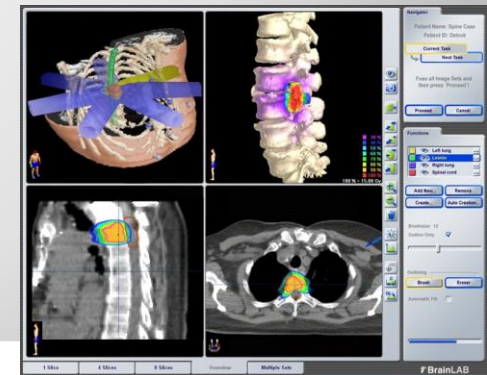


Ο ΟΡΟΣ ΣΤΕΡΕΟΤΑΚΤΙΚΗ
(ΜΕ ΤΗΝ ΑΚΡΙΒΕΙΑ ΤΟΥ ΟΡΟΥ)
ΣΤΗΝ ΟΥΣΙΑ
ΔΕΝ ΕΙΝΑΙ ΠΛΕΟΝ ΔΟΚΙΜΟΣ!!!
(επιστημονικά....)



ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

- SBRT has been defined by the American College of Radiology (ACR) and American Society for Radiation Oncology (ASTRO)
- as the use of very large doses of radiation,
- defined as >6 Gy/fraction given over few (five or fewer) fractions.
- SBRT has unique radiobiological characteristics, which can cause dramatic tumor response, leading to the associated term "ablative" radiotherapy.



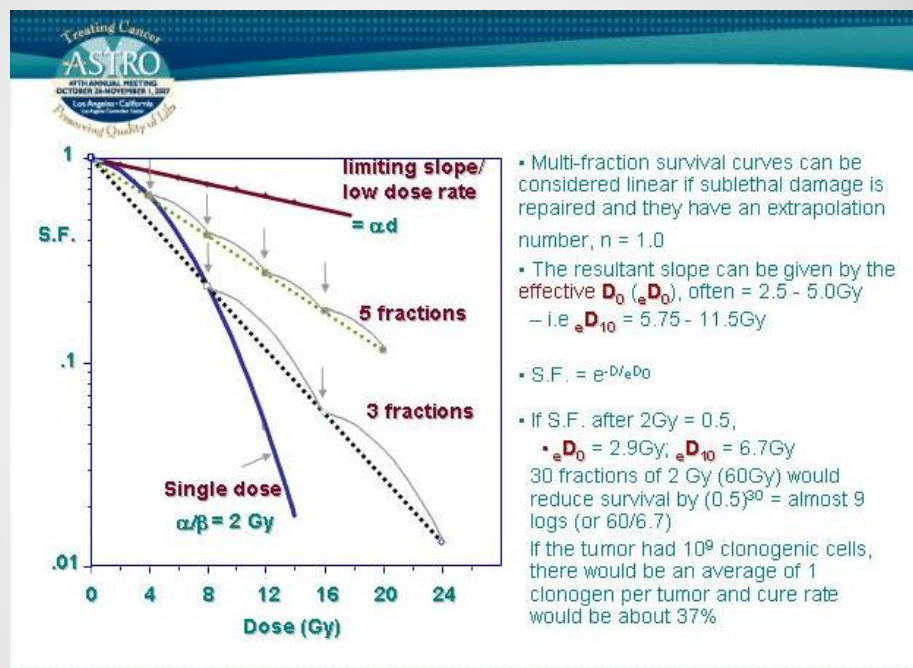
Definitions

- **Radiosurgery**

- High dose of radiation
- Generally delivered in one fraction
- Considered ablative
 - Generally yields high rate of local control
 - *akin to a surgical resection without the use of a knife*

.....Εως 5

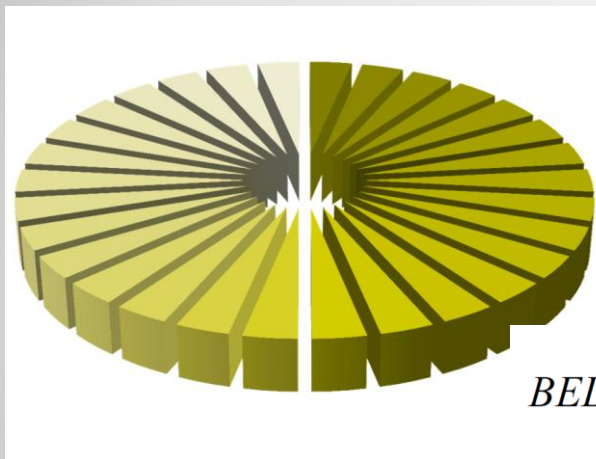
ΔΡΑΣΗ ΤΗΣ ΑΚΤΙΝΟΒΟΛΙΑΣ ΑΝΑΛΟΓΑ ΜΕ ΤΟΝ ΤΡΟΠΟ ΧΟΡΗΓΗΣΗΣ



**ΔΙΑΦΟΡΕΤΙΚΗ ΔΟΣΗ ΓΙΑ ΤΟ ΙΔΙΟ ΑΠΟΤΕΛΕΣΜΑ
ΑΝΑΛΟΓΑ ΜΕ ΔΙΑΦΟΡΕΤΙΚΗ ΚΛΑΣΜΑΤΟΠΟΙΗΣΗ**

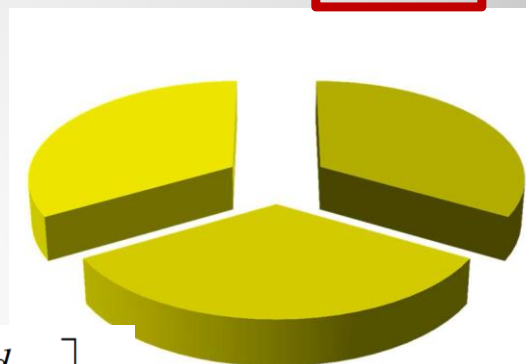
Δόση και βιολογικά ισοδύναμη δόση

Conventional: 60 Gy



30 fx of 2 Gy
 $BED_{10}=60. [1+2/10]=72 \text{ Gy}$

SABR: 60Gy



3 fx of 20 Gy
 $BED_{10}=60. [1+20/10]=180 \text{ Gy}$

$$BED = Nd \left[1 + \frac{d}{(\alpha / \beta)} \right]$$

**Improved local control and survival
are associated with SBRT regimens whose BED is >100 Gy.**

ΔΙΑΦΟΡΕΣ ΣΤΙΣ ΑΡΧΕΣ ΤΩΝ ΜΕΘΟΔΩΝ

ΑΡΧΕΣ ΣΤΕΡΕΟΤΑΚΤΙΚΗΣ
ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:

ΜΟΝΟ ΟΡΑΤΟΣ ΟΓΚΟΣ



ΑΡΧΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:
ΚΑΙ ΠΕΡΙΟΧΕΣ ΠΟΥ ΥΠΟΘΕΤΕΙΣ ΌΤΙ ΜΠΟΡΕΙ ΝΑ ΥΠΑΡΧΟΥΝ ΚΥΤΤΑΡΑ

ΔΙΑΦΟΡΕΣ ΣΤΙΣ ΑΡΧΕΣ ΤΩΝ ΜΕΘΟΔΩΝ

**ΑΡΧΕΣ ΣΤΕΡΕΟΤΑΚΤΙΚΗΣ
ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:**

ΜΟΝΟ ΟΡΑΤΟΣ ΟΓΚΟΣ



**ΟΣΟ ΠΕΡΙΣΣΟΤΕΡΟ
ΦΥΣΙΟΛΟΓΙΚΟ ΙΣΤΟ
ΕΧΕΙ ΤΟ ΠΕΔΙΟ ΑΚΤΙΝΟΒΟΛΗΣΗΣ
ΤΟΣΟ ΠΕΡΙΟΡΙΖΕΤΑΙ ΚΑΙ Η ΔΟΣΗ**

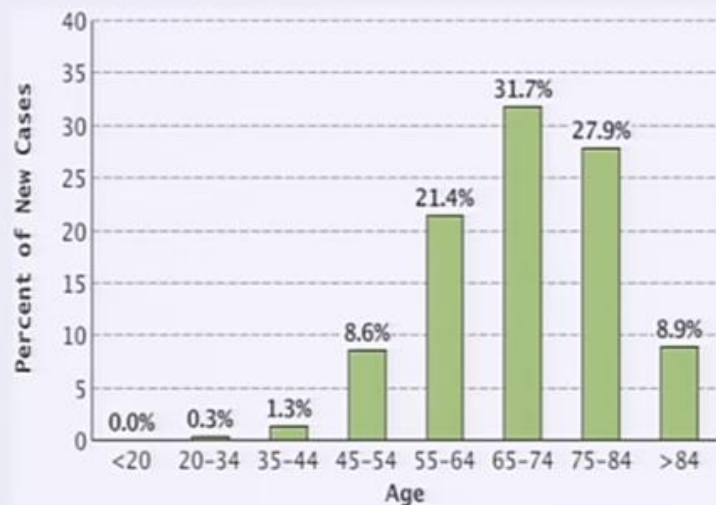


**ΑΡΧΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:
ΚΑΙ ΠΕΡΙΟΧΕΣ ΠΟΥ ΥΠΟΘΕΤΕΙΣ ΌΤΙ ΜΠΟΡΕΙ ΝΑ ΥΠΑΡΧΟΥΝ ΚΥΤΤΑΡΑ**



ΣΤΑΤΙΣΤΙΚΑ ΚΑΡΚΙΝΟΥ ΠΝΕΥΜΟΝΑ

Percent of New Cases by Age Group: Lung and Bronchus Cancer



Lung and bronchus cancer is most frequently diagnosed among people aged 65-74.

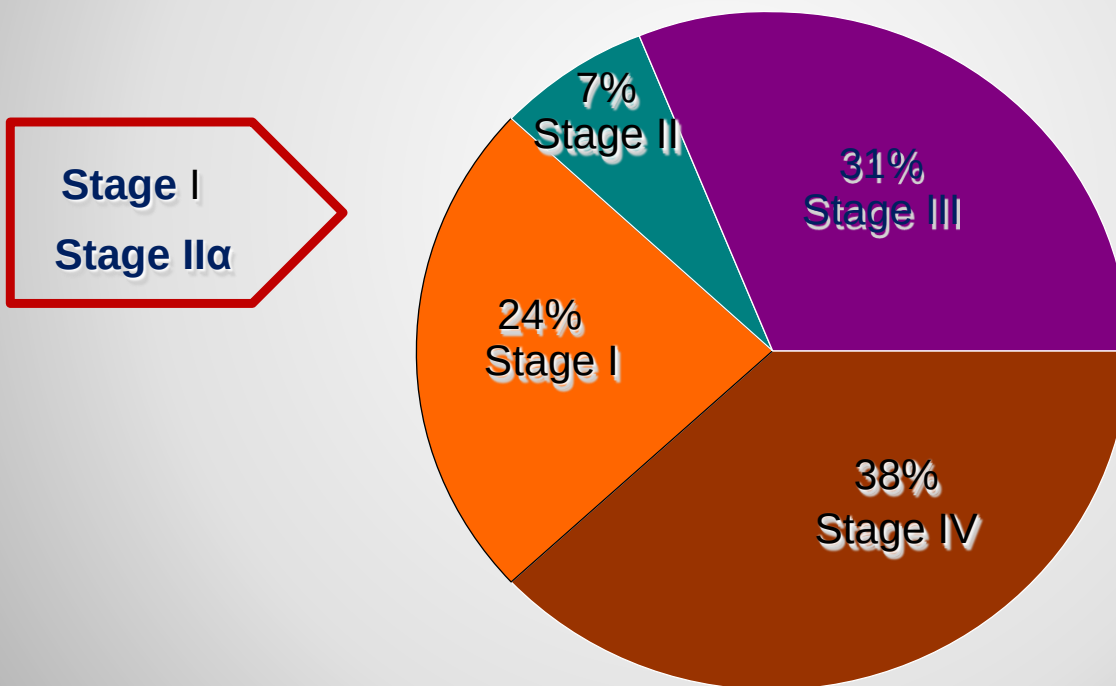
Median Age
At Diagnosis

70

SEER 18 2007-2011, All Races, Both Sexes

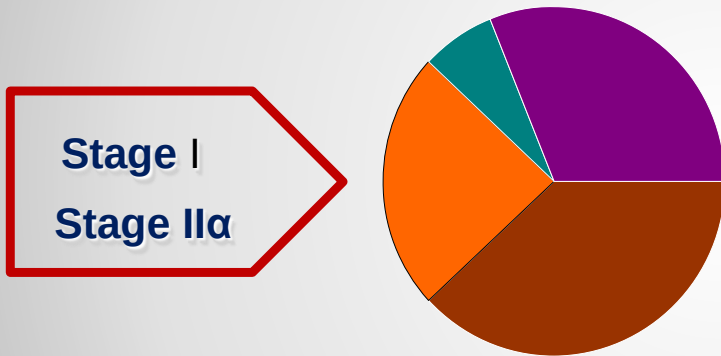
ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

Πρώιμα Στάδια Μη Μικροκυτταρικού Καρκίνου του Πνεύμονα



ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

Πρώιμα Στάδια Μη Μικροκυτταρικού Καρκίνου του Πνεύμονα



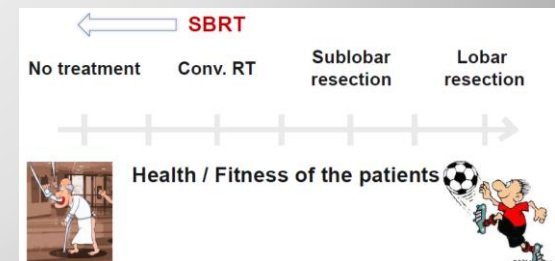
ΘΕΡΑΠΕΙΑ ΕΚΛΟΓΗΣ
είναι η χειρουργική αφαίρεση

Πρώιμο Στάδιο Μη Μικροκυτταρικού Καρκίνου του Πνεύμονα

ΘΕΡΑΠΕΙΑ ΕΚΛΟΓΗΣ είναι η χειρουργική αφαίρεση

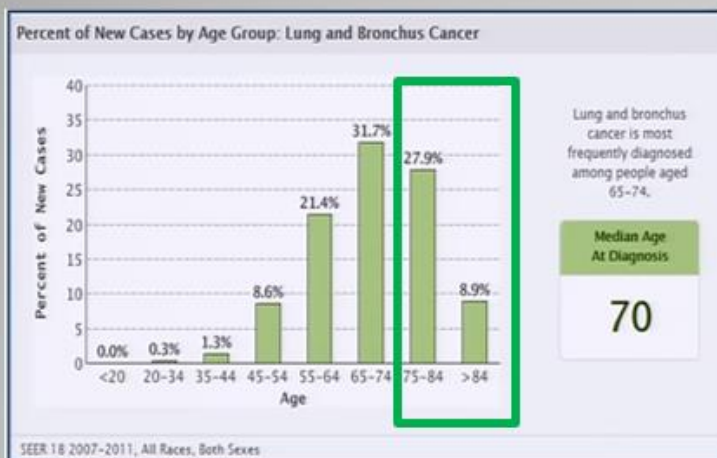
Κάποιοι ασθενείς (κυρίως μεγαλύτερης ηλικίας)
δεν μπορούν να υποβληθούν σε χειρουργική εξαίρεση
λόγω συνοδών προβλημάτων
όπως ΧΑΠ ή καρδιολογικών - καρδιαγγειακών
νοσημάτων...

Ή δε το επιθυμούν...





ΣΤΑΤΙΣΤΙΚΑ ΚΑΡΚΙΝΟΥ ΠΝΕΥΜΟΝΑ



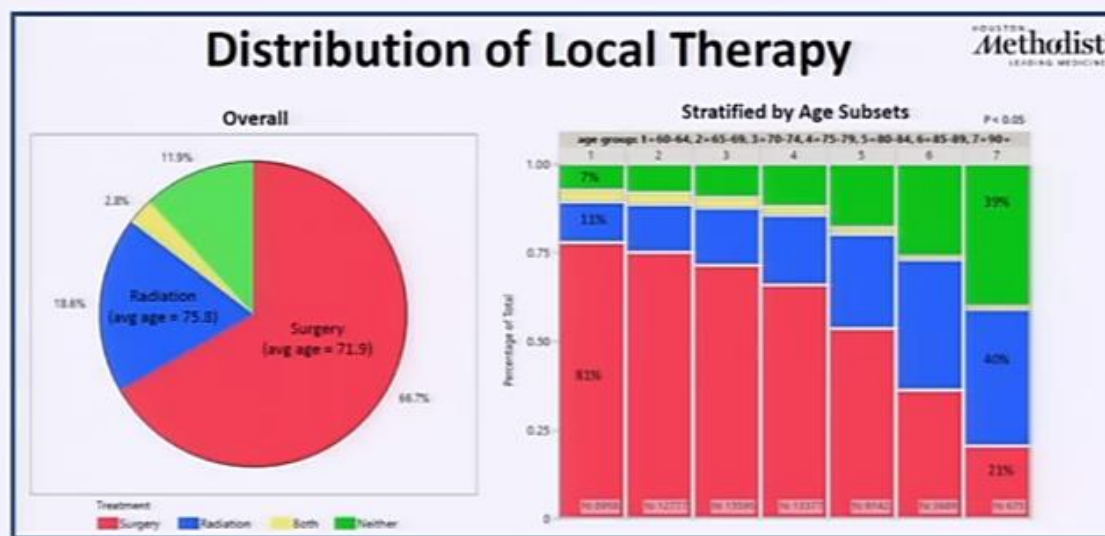
**ΚΑΠΟΙΟΙ ΘΜΩΣ
ΔΕΝ ΜΠΟΡΟΥΝ
ΝΑ ΥΠΟΒΛΗΘΟΥΝ ΣΕ ΧΕΙΡΟΥΡΓΕΙΟ
ΚΥΡΙΩΣ ΜΕΓΑΛΥΤΕΡΗΣ ΗΛΙΚΙΑΣ**

- Αρχικό FEV1<40%
- Πιθανό μετεγχειρητικό FEV1<30%
- Υποξαιμία ($pO_2 < 70$ mmHg)
- Υπερκαπνία ($pCO_2 > 50$ mmHg)
- Καρδιολογικά προβλήματα
- Ηλικία
- Δυσκολίες κατά την αναισθησία
- Δύσκολη μετεγχειρητική ανάνηψη



ΣΤΑΤΙΣΤΙΚΑ ΚΑΡΚΙΝΟΥ ΠΝΕΥΜΟΝΑ

Outcomes in Elderly Stage I Non-Small Cell Lung Cancer in the SBRT Era: A SEER Analysis



Click

SM Dalwadi, Abstract 152. ASTRO 16

ASTRO 2016

.....ΠΑΡΑΚΟΛΟΥΘΗΣΗ

ΣΤΑ ΑΡΧΙΚΑ ΣΤΑΔΙΑ

ΣΕ ΑΥΤΟΥΣ ΠΟΥ ΔΕΝ ΜΠΟΡΟΥΝ ΝΑ ΥΠΟΒΛΗΘΟΥΝ ΣΕ ΧΕΙΡΟΥΡΓΕΙΟ

Observation-Only Management of Early Stage, Medically Inoperable Lung Cancer: Poor Outcome



Not much data to guide us but.....

- RAZ et al¹- Analysis of California Cancer Registry 1989-2003
 - 1432 cases (total 19702) Stage I NSCLC received no treatment
 - Median Survival 9 months (13 months T1 alone)
 - 5 year OS 6% (T1=9%)
- McGarry et al²
 - Small study ~130 patients but >50% of untreated patients with early stage NSCLC died of their cancer.

Raz DJ et al. Chest; 2007, 132: 193-9
Mc Garry RC et al, Chest; 2002, 121: 1155-8

Η ΠΡΟΓΝΩΣΗ ΕΙΝΑΙ ΠΟΛΥ ΠΤΩΧΗ ...

ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ Vς ΧΕΙΡΟΥΡΓΕΙΟ

ΜΗ ΙΣΟΔΥΝΑΜΑ ΑΠΟΤΕΛΕΣΜΑΤΑ

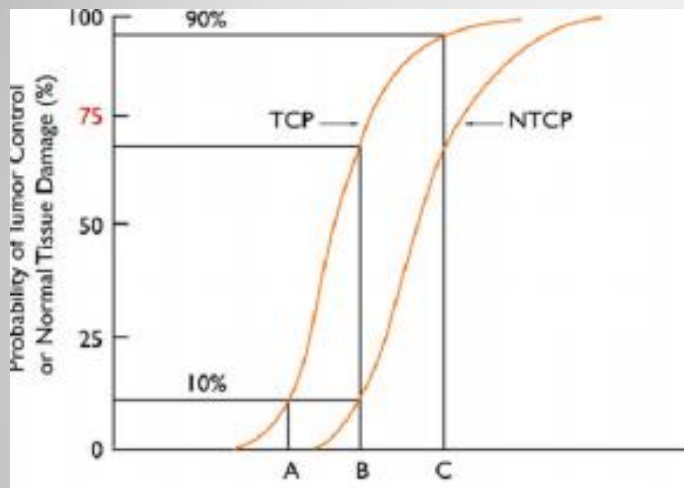
3-5 Year Outcome in Early Stage Lung Cancer

	<u>Rx Modality</u>	<u>% alive</u>
• Stage I	Surgery	60-80%
Stage I*	Conventional XRT	15-45%

*clinically staged and mostly medically inoperable
(some refused surgery)

Conventional RT generally 60-66 Gy delivered in 6-7 weeks

Η ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ ΤΗΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ ΕΧΕΙ ΣΧΕΣΗ ΜΕ ΤΗΝ ΔΟΣΗ

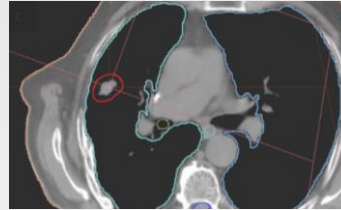


ΜΗΠΩΣ ΥΨΗΛΟΤΕΡΕΣ ΔΟΣΕΙΣ;

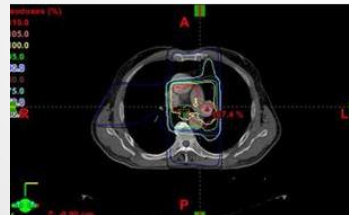
ΥΨΗΛΟΤΕΡΕΣ ΔΟΣΕΙΣ:

**ΠΙΟ ΑΠΟΤΕΛΕΣΜΑΤΙΚΕΣ ΓΙΑ ΤΟΝ ΟΓΚΟ
ΑΛΛΑ
ΠΙΟ ΤΟΞΙΚΕΣ ΓΙΑ ΤΟΥΣ ΦΥΣΙΟΛΟΓΙΚΟΥΣ ΙΣΤΟΥΣ**

ΔΙΑΦΟΡΕΣ ΣΤΙΣ ΑΡΧΕΣ ΤΩΝ ΜΕΘΟΔΩΝ



ΑΡΧΕΣ ΣΤΕΡΕΟΤΑΚΤΙΚΗΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:



ΑΡΧΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ:

ΟΣΟ ΟΜΩΣ ΜΕΓΑΛΩΝΕΙ Η ΠΕΡΙΟΧΗ ΑΚΤΙΝΟΒΟΛΗΣΗΣ
ΤΟΣΟ ΠΡΕΠΕΙ ΝΑ ΠΕΡΙΟΡΙΖΕΤΑΙ Η ΔΟΣΗ

ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ: ΑΝΑΖΗΤΗΣΗ ΣΩΣΤΗΣ ΔΟΣΗΣ

Extracranial Stereotactic Radioablation*

Results of a Phase I Study in Medically Inoperable Stage I Non-small Cell Lung Cancer

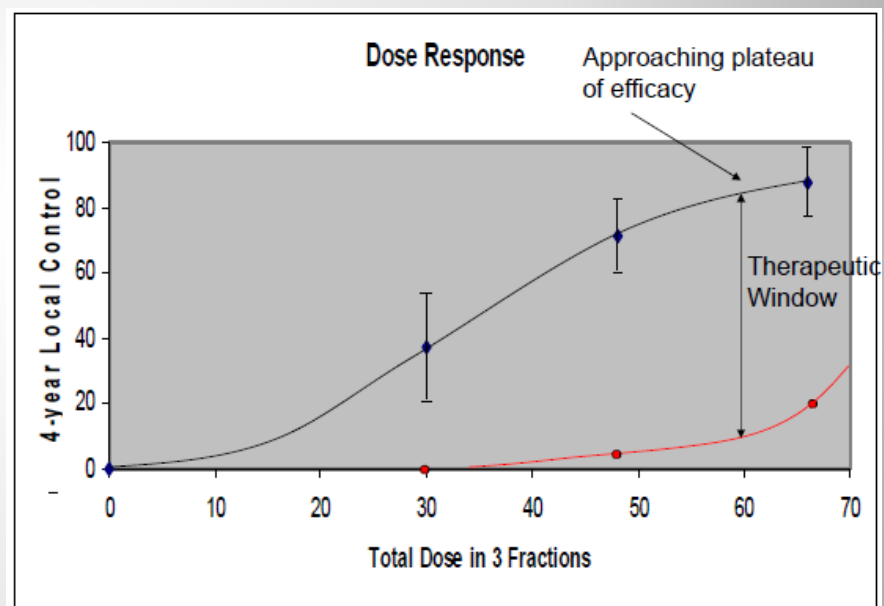
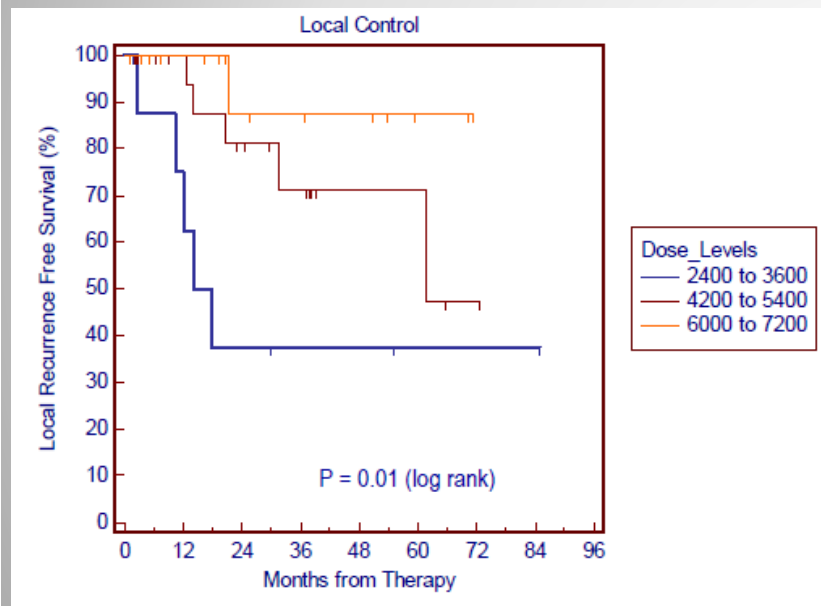
*Robert Timmerman, MD; Lech Papiez, PhD; Ronald McGarry, MD;
Laura Likes, RT; Colleen DesRosiers, MS; Stephanie Frost, MS; and
Mark Williams, MD*

- Classic phase I design
- Low starting dose 8 Gy X 3 = 24 Gy
- Dose escalation to very high doses 20-24 Gy X 3 = 60-72 Gy

(CHEST 2003; 124:1946-1955)

Extracranial Stereotactic Radioablation*

Results of a Phase I Study in Medically Inoperable Stage I Non-small Cell Lung Cancer



(CHEST 2003; 124:1946-1955)

ΑΠΟ ΤΙΣ ΠΡΩΤΕΣ ΜΕΛΕΤΕΣ RTOG 0236

- First North American cooperative group trial using Stereotactic Body Radiation Therapy (SBRT).

Long-term Results of RTOG 0236:
A Phase II Trial of SBRT in the Treatment of
Patients with Medically Inoperable Stage I
Non-small Cell Lung Cancer

R. Timmerman¹; C. Hu²; J. Michalski³; W. Straube³; J. Galvin⁴;
D. Johnstone⁵; J. Bradley³; R. Barriger⁶; A. Bezjak⁷; G. Videtic⁸;
L. Nedzi¹; M. Werner-Wasik⁴; Y. Chen⁹; R. Komaki¹⁰; H. Choy¹

¹University of Texas Southwestern Medical Center, Dallas, TX;
²American College of Radiology, Philadelphia, PA; ³Washington University, St. Louis, MO;
⁴The Jefferson Hospital, Philadelphia, PA; ⁵Medical College of Wisconsin, Milwaukee, WI;
⁶Indiana University, Indianapolis, IN; ⁷Princess Margaret Hospital, Toronto, ON;
⁸Cleveland Clinic, Cleveland, OH; ⁹University of Rochester Medical Center, Rochester, NY;
¹⁰MD Anderson Cancer Ctr., Houston, TX

The Radiation Therapy Oncology Group (now called the NRG) is supported by grants U10CA21661, U10CA180868, U10CA180822, U10 CA37422, U24CA180803 from the National Cancer Institute

- 59 frail patients
- Medical problems preclude surgery, e.g.:
 - Emphysema
 - Heart disease
 - Stroke

- First presented in 2009 (ASTRO) and published in 2010 (JAMA) leading to a significant transition in routine care

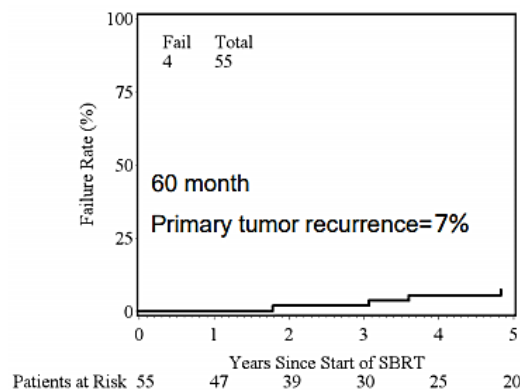
ΑΠΟ ΤΙΣ ΠΡΩΤΕΣ ΜΕΛΕΤΕΣ RTOG 0236

Results

Median follow-up 4 years (7.2 years for survivors)

Irradiated Tumors Well Controlled

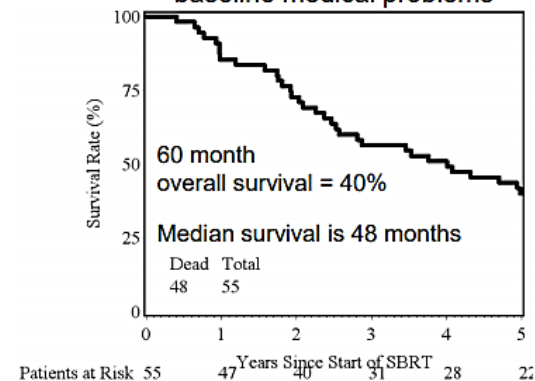
Owing to Potent Therapy



ΤΟΠΙΚΟΣ ΕΛΕΓΧΟΣ

Overall Survival Good but Declining

Partly related to
baseline medical problems



ΕΠΙΒΙΩΣΗ

ΑΠΟ ΤΙΣ ΠΡΩΤΕΣ ΜΕΛΕΤΕΣ RTOG 0236

Conclusions

- Primary tumor recurrence (treated area) remained very low at 5 years (7%) owing to the potent SBRT regimen.
▪ Primary control similar to surgery **ΤΟΠΙΚΗ ΥΠΟΤΡΟΠΗ 7%**
- Local-regional failure increased (38% at 5 years compared to 13% at 3 years), due to late failures (up to 6 years post SBRT) in mostly the involved lobe but also the hilum, and mediastinum (all untreated).
▪ ? Need better staging or effective adjuvant therapy **ΤΟΠΙΚΟΠΕΡΙΟΧΙΚΗ ΥΠΟΤΡΟΠΗ ΣΤΗΝ 3ΕΤΙΑ 13%**
ΣΤΗΝ 5ΕΤΙΑ 38%
- Severe toxicity remained relatively unchanged with longer follow-up.
▪ Progressive “late” toxicity did not occur **ΧΩΡΙΣ ΙΔΙΑΙΤΕΡΗ ΤΟΞΙΚΟΤΗΤΑ ΚΑΙ ΣΤΟ ΜΑΚΡΟ FU**
- Disease free and overall survival in this medically inoperable population at 5 years was 26% and 40%, respectively.
ΕΛΕΥΘΕΡΟ ΝΟΣΟΥ ΣΤΗΝ 5ΕΤΙΑ 26%
ΕΠΙΒΙΩΣΗ ΣΤΗΝ 5ΕΤΙΑ 40%

Στερεοτακτική Ακτινοθεραπεία σε Μη Εξαιρέσιμο (για ιατρικούς λόγους) ΜΜΚΠ Σταδίου I/II

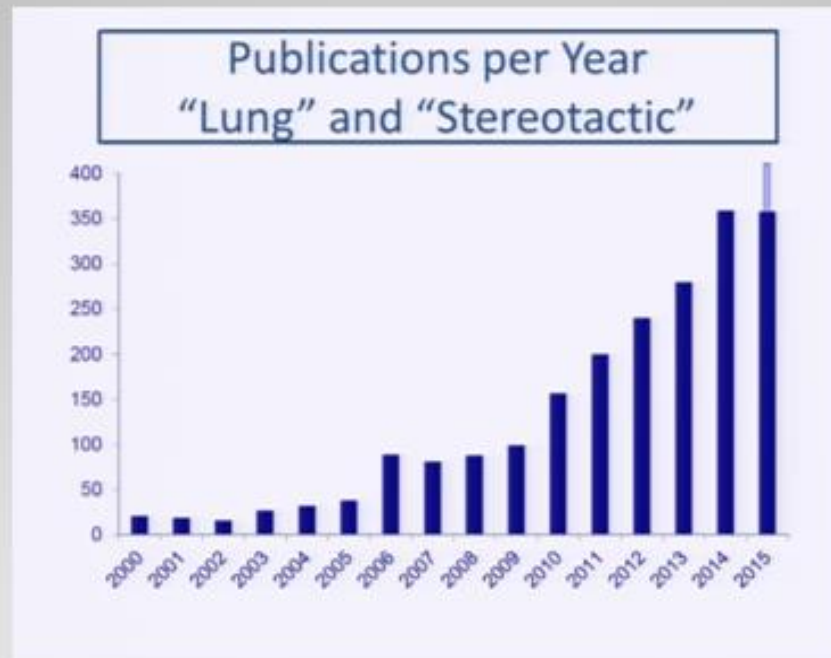
Prospective Phase II Studies on SABR in NSCLC

	N pts	Median Fup	SABR dose	Local Control	OS
Nagata et al. 2005	45	30 months	12 Gy x 4 fr @ isocenter	30mo 98%	3-yr 75%
Baumann et al. 2009	57	35 months	15 Gy x 3 fr @ 65%	3-yr 92%	3-yr 60%
Fakiris et al. 2009	70	50 months	20-22 Gy x 3 fr @ 80%	3-yr 88%	3-yr 43%
Ricardi et al. 2010	62	28 months	15 Gy x 3 fr @ 80%	3-yr 88%	3-yr 43%
Timmerman et al. 2010	54	34 months	18 Gy x 3 fr @ 80%	3-yr 98%	3-yr 60%
Bral et al. 2011	40	16 months	3-4 fr td 60 Gy	2-yr 84%	2-yr 43%

Author	No. of Patients.	Local Control	Overall Survival (OS)
Nagata et al. 2005 [12]	45	95% at 5 years	83% at 5 years
Onishi et al. 2007 [13]	257	86% at 3 years	56% at 3 years
Lagerwaard et al. 2008 [14]	206	93% at 2 years	64% at 2 years
Haasbeek et al. 2010 [15]	193	89.3% at 3 years	45.1% at 3 years
Bongers et al. 2011 [16]	500	90.4% at 3 years	53.1% at 3 years
Palma et al. 2012 [17]	176	89% at 3 years	47% at 3 years
Senthi et al. 2012 [18]	676	10.5% LRR at 5 years	Not available
Chang et al. 2012 [19]	130	98.5% at 2 years	65.3% at 3 years
Gillespie et al. 2015 [20]	320	95% at 2 years	64.25% at 2 years
Murray et al. 2015 [21]	273	95.7% at 3 years	38.6% at 3 years
Shaverdian et al. 2016 [22]	118	97% at 3 years	77% at 3 years
Chiang et al. 2016 [23]	192	89.3% at 3 years	72.4% at 3 years

....ΠΑΡΑ ΠΟΛΛΕΣ ΟΙ ΜΕΛΕΤΕΣ..

Στερεοτακτική Ακτινοθεραπεία



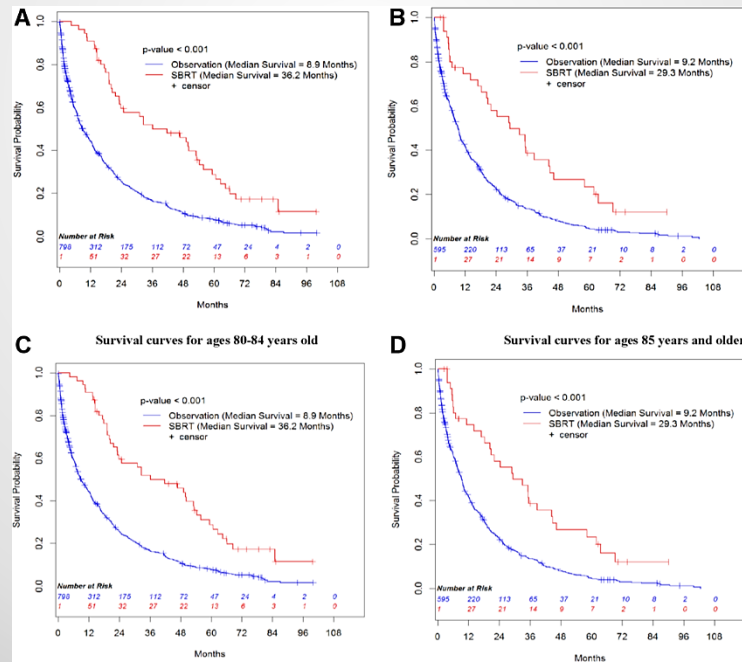
ΑΚΤΙΝΟΧΕΙΡΟΥΡΓΙΚΗ VS ΜΗ ΘΕΡΑΠΕΙΑ

Original Article

Stereotactic Body Radiation Therapy Versus No Treatment for Early Stage Non-Small Cell Lung Cancer in Medically Inoperable Elderly Patients: A National Cancer Data Base Analysis

Ronica H. Nanda, MD^{1,2}; Yuan Liu, PhD^{2,3,4}; Theresa W. Gillespie, PhD^{2,3}; John L. Mikell, MD^{1,2}; Suresh S. Ramalingam, MD^{2,5}; Felix G. Fernandez, MD^{2,6}; Walter J. Curran, MD^{1,2}; Joseph Lipscomb, PhD^{2,4}; and Kristin A. Higgins, MD^{1,2}

ΗΛΙΚΙΑ 70-74
8.9 vs 36.2 ΜΗΝΕΣ



ΗΛΙΚΙΑ >85
9.2 vs 28.3 ΜΗΝΕΣ

CANCER 2015

Practice Patterns and Outcomes in Elderly Stage I Non-Small-cell Lung Cancer: A 2004 to 2012 SEER Analysis

This study was presented in part at the 2016 American Society for Radiation Oncology Annual Meeting, Lung – Stereotactic Body Radiation Therapy Scientific Session.

[Shraddha M. Dalwadi¹](#), [Sean S. Szeja²](#), [Eric H. Bernicker³](#), [E. Brian Butler³](#), [Bin S. Teh³](#), [Andrew M. Farach³](#)  



Conclusion

- With advancing age, radiation replaces surgery as the most appropriate treatment modality for early-stage NSCLC.
- Concurrent with the adoption of SBRT as a community standard, survival has improved significantly between 2004-2011 for patients treated with radiation only.
 - OS at 23 months increased **19%**
 - CSS at 23 months increased **24%**

EINAI H AKTINOXEIPOYPTIKH TO... “STANDARD OF CARE”;

Is SBRT a New Standard of Care in Inoperable Lung Cancer?

Maria Sgambati, MD

Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer

Robert Timmerman; Rebecca Paulus; James Galvin; et al.

JAMA. 2010;303(11):1070-1076 (doi:10.1001/jama.2010.261)

- SBRT has become a standard of care for medically inoperable patients
 - No randomized trial deemed necessary
 - Up to 10,000 patients per year in US

JAMA. 2010

ΟΜΩΣ ΠΡΑΓΜΑΤΙΚΑ ΥΠΕΡΕΧΕΙ Η ΣΤΕΡΕΟΤΑΚΤΙΚΗ....

ΣΕ ΣΥΓΚΡΙΣΗ ΜΕ ΤΗΝ ΚΛΑΣΣΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ;

- Τοπικός έλεγχος

- SBRT 54 Gy in 3 fx, **98%** (τοπικός έλεγχος), 91% (lobe) (*RTOG 0236*)
- EBRT 60-66 Gy / 30-33 fx, **~50%** (*Qiao, Lung Cancer 2003*)

Beaumont experience (*Lanni, Am J Clin Oncol 2011*)

- SBRT (48-60 Gy in 4-5 fx, n=45) vs. EBRT (70 Gy/ 35 fx, n=41)
- 3y LC, **88% vs. 66%** (p=0.10)

- Μεταανάλυση (*Grutters, Radiother Oncol 2010*)

- SBRT (n=895) vs. EBRT (n=1326)
- 2-year OS, **70% vs. 53%** (p=<0.001)
- 2-year DFS, **83.4% vs. 67.4%** (p=0.006)

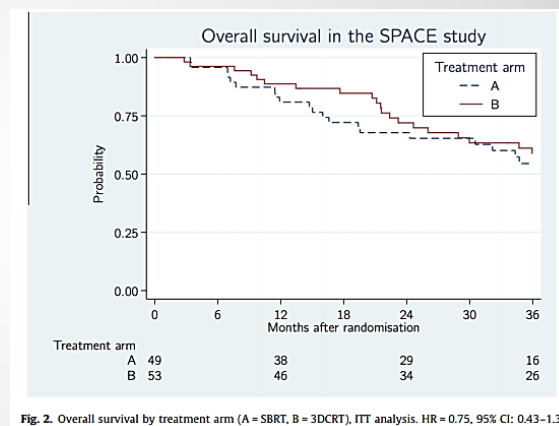
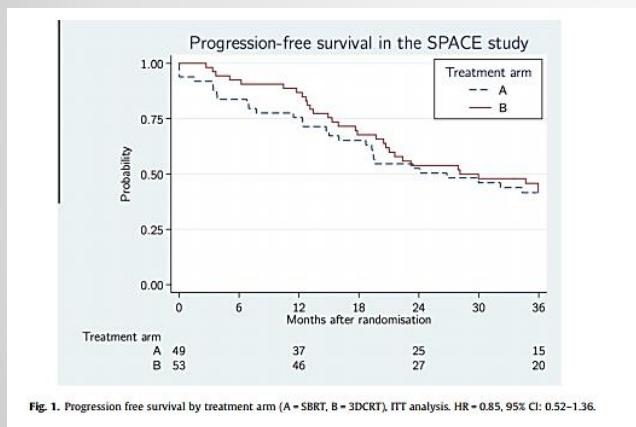
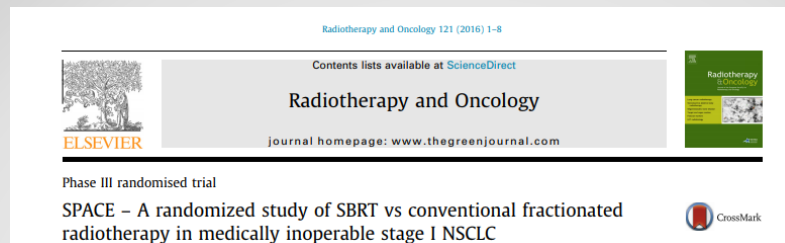
**ΟΜΩΣ ΠΡΑΓΜΑΤΙΚΑ
ΥΠΕΡΕΧΕΙ Η ΣΤΕΡΕΟΤΑΚΤΙΚΗ....**

**ΣΕ ΣΥΓΚΡΙΣΗ
ΜΕ ΤΗΝ ΚΛΑΣΣΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ;**

Randomised trials of conventional radiotherapy versus SABR

	SPACE NCT019207	CHISEL NCT01014130
Study arms	SABR: 66 Gy in 3 fractions (to isocenter) CFRT: 66 Gy (2Gy fractions)	54 Gy in 3 fractions CFRT: 60-66Gy (2Gy fractions)
Primary End- point	Freedom from tumor progression at 36 months	Time to Local Failure at 24 months
Secondary end- points	OS at 36 months Toxicity, QoL	OS, CSS, Toxicity QoL
Total enrolled	102 patients (completed)	100 patients (76 enrolled)

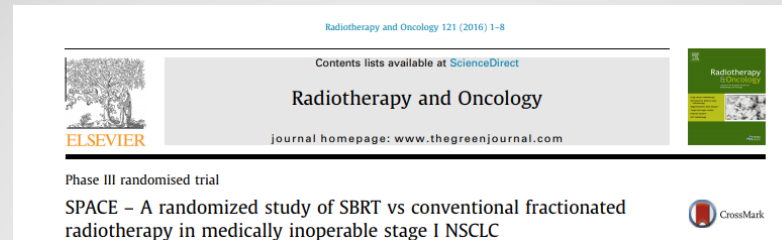
SPACE



ΤΟΠΙΚΟΣ ΕΛΕΓΧΟΣ

ΕΠΙΒΙΩΣΗ

SPACE



Interpretation: There was no difference in PFS and OS between SBRT and conventionally treated patients despite an imbalance of prognostic factors. We observed a tendency of an improved disease control rate in the SBRT group and they experienced better HRQL and less toxicity. SBRT is convenient for patients and should be considered standard treatment for patients with inoperable stage I NSCLC.

© 2016 Elsevier Ireland Ltd. All rights reserved. Radiotherapy and Oncology 121 (2016) 1-8

CHISEL

THE LANCET Oncology

Volume 20, Issue 4, April 2019, Pages 494-503

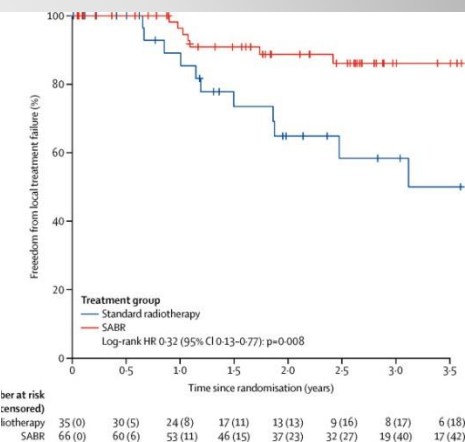


Articles

Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial

Interpretation

In patients with inoperable peripherally located stage 1 NSCLC, compared with standard radiotherapy, SABR resulted in superior local control of the primary disease without an increase in major toxicity.



ΤΟΠΙΚΟΣ ΕΛΕΓΧΟΣ

The findings of this trial suggest that SABR should be the treatment of choice for this patient group.

APRIL 2019

**.....ΑΛΛΑ ΥΠΑΡΧΕΙ ΚΑΙ
Η ΣΚΟΤΕΙΝΗ ΠΛΕΥΡΑ ΤΟΥ ΦΕΓΓΑΡΙΟΥ**



ΤΟΞΙΚΟΤΗΤΑ

Excessive Toxicity When Treating Central Tumors in a Phase II Study of Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Lung Cancer

Robert Timmerman, Ronald McGarry, Constantin Yiannoutsos, Lech Papiez, Kathy Tudor, Jill DeLuca, Marvene Ewing, Ranzzi Abdulrahman, Colleen DesRosiers, Mark Williams, and James Fletcher

- Phase II: Indiana University
 - T1 N0: 2000 cGy x 3 fractions
 - T2 N0: 2200 cGy x 3 fractions
- 70 patients (< 7 cm)
 - medically inoperable
- 95% 2-yr Local Tumor Control (88% 3-yr)
- Median Survival = 32.6 months

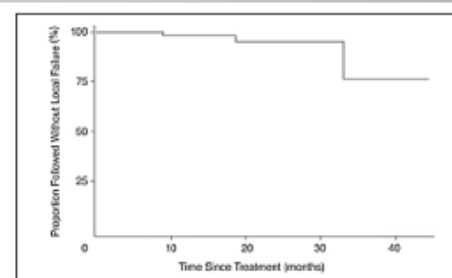


Fig 1. Kaplan-Meier plot of time from treatment until local failure (percent with local control).

ΤΟΠΙΚΟΣ ΕΛΕΓΧΟΣ

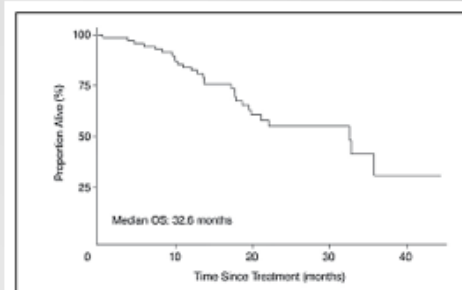


Fig 2. Kaplan-Meier plot of overall survival (OS).

ΕΠΙΒΙΩΣΗ

Excessive Toxicity When Treating Central Tumors in a Phase II Study of Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Lung Cancer

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- 70 patients (< 7 cm)
 - medically inoperable
- 95% 2-yr Local Tumor Control (88% 3-yr)
- Median Survival = 32.6 months

Grade 3+ toxicity (60 -66 Gy / 3 fx):

- 27% for Central lesions
- 10% for Peripheral lesions
- 5 deaths *potentially* treatment related (n=70)

Zone of the Proximal Bronchial Tree

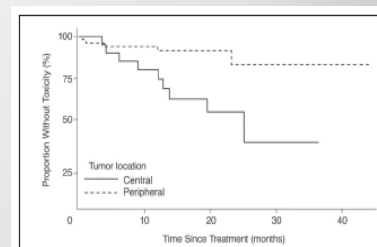
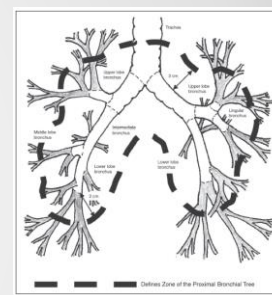


Fig 4. Kaplan-Meier plot of time from treatment until grade 3 to 5 treatment related toxicity comparing patients with tumors in the central (perihilar and central mediastinal) regions from those with more peripheral tumors.



Lung Cancer

Volume 123, September 2018, Pages 142-148



Review

Stereotactic ablative radiotherapy (SABR) for early-stage central lung tumors: New insights and approaches

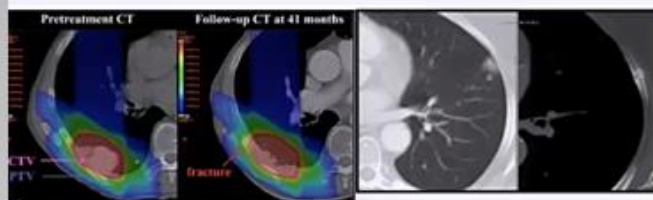
H. Tekatli , F.O.B. Spoelstra, M. Palacios, J. van Sornsen de Koste, B.J. Slotman, S. Senan

- A high toxicity is seen when ultracentral tumors are treated using SABR.
- Conventional radiotherapy appears more appropriate in ultracentral tumors.

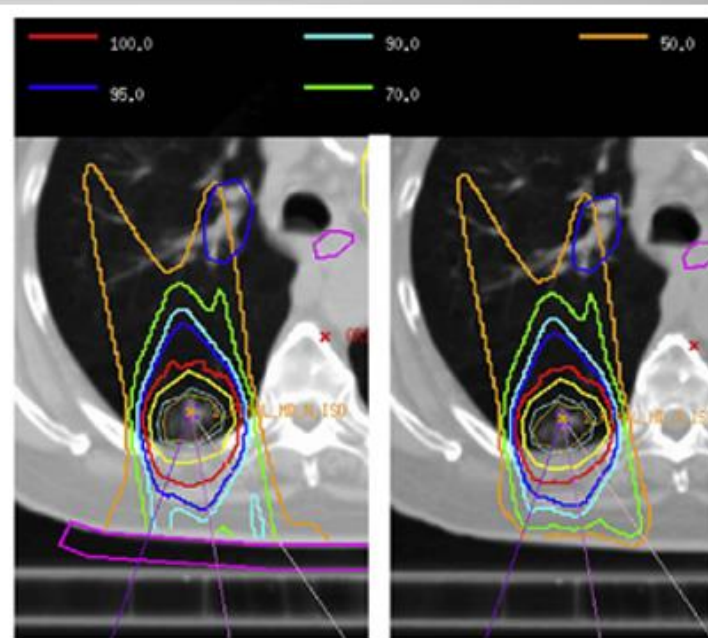
- ΠΟΛΥ ΠΕΡΙΦΕΡΙΚΟΙ ΟΓΚΟΙ

Παρενέργειες - Επιπλοκές

Very Peripheral Lesions

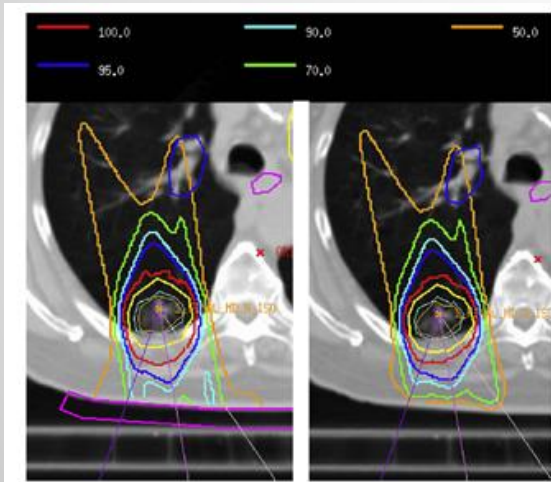


STUDY	event	notes
Petterson	7 / 33 rib fx	2 cm 3 dose
Voroney	9 / 42 rib fx	Median 17 months to fx
Dunlap	13 / 31 pain	Volume > 30 Gy
Bongers	Gr 3 pain, fx	Vol>30 Gy, 50 Gy, max
Stephans	10 / 134 pain	Vol > 30 Gy, > 60 Gy
Mutter	39% G2 2+ sx	70 cc> 30 Gy ⁶⁰



- **ΠΟΛΥ ΠΕΡΙΦΕΡΙΚΟΙ ΟΓΚΟΙ**

Παρενέργειες - Επιπλοκές



- **ΠΟΛΥ ΚΕΝΤΡΙΚΟΙ ..ΠΟΛΥ ΠΕΡΙΦΕΡΙΚΟΙ ΟΓΚΟΙ**

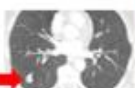
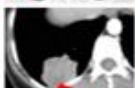
Παρενέργειες - Επιπλοκές



ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΠΝΕΥΜΟΝΟΣ –ΤΟΞΙΚΟΤΗΤΑ:

Η λύση είναι η μεγαλύτερη κλασματοποίηση:

ESTRO ACROP recommendation

	Consensus fractionation	BED10
 Peripheral location	3 x 15Gy	113Gy BED10
 Broad chest wall contact	4 x 12Gy	107 Gy BED10
 Central location	8 x 7.5Gy	105 Gy BED10

Fractionation Schedules

T1 peripheral tumors (≤ 3 cm),

- 3 fractions of 18 Gy

T2 tumors (or T1 tumors with broad contact with the chest wall)

- 5 fractions of 11 Gy

High-risk tumors adjacent to pericardium, mediastinum, hilus or brachial plexus

- 8 fractions of 7.5 Gy
- 5 fractions of 11.5 - 12 Gy

All schedules BED10 >100Gy

Ultra-central tumors

- 12 fractions of 5 Gy

ESMO Recommended Dose: BED >100 Gy

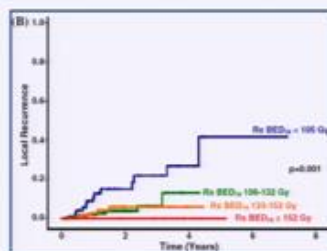


Table 2. Commonly Used Doses for SABR

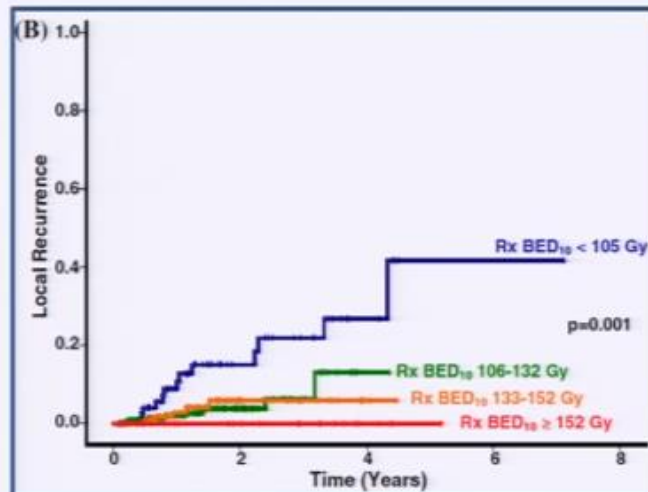
Total Dose	# Fractions	Example Indications
25-34 Gy	1	Peripheral, small (<2 cm) tumors, esp. >1 cm from chest wall
45-60 Gy	3	Peripheral tumors and >1 cm from chest wall
48-50 Gy	4	Central or peripheral tumors <4-5 cm, especially <1 cm from chest wall
50-55 Gy	5	Central or peripheral tumors, especially <1 cm from chest wall
60-70 Gy	8-10	Central tumors

ASTRO Executive Summary of Lung SBRT Guidelines

- SBRT directed toward centrally located lung tumors carries unique and significant risks when compared to treatment directed at peripherally located tumors. The use of 3-fraction regimens should be avoided in this setting.
- SBRT directed at central lung tumors should be delivered in 4 or 5 fractions. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment. For central tumors for which SBRT is deemed too high risk, hypofractionated radiation therapy utilizing 6 to 15 fractions can be considered.

**ΑΥΤΟ ΟΜΩΣ ΠΟΥ ΕΙΝΑΙ ΠΟΛΥ ΒΑΣΙΚΟ
ΕΙΝΑΙ
Η ΒΙΟΛΟΓΙΚΑ ΑΠΟΤΕΛΕΣΜΑΤΙΚΗ ΔΟΣΗ ΝΑ ΕΙΝΑΙ ΥΨΗΛΗ!!**

ESMO Recommended Dose: BED >100 Gy



ΕΡΩΤΗΜΑ: ΜΗΠΩΣ ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΚΑΙ ΣΤΟΥΣ ΑΣΘΕΝΕΙΣ ΠΟΥ ΜΠΟΡΟΥΝ ΝΑ ΧΕΙΡΟΥΡΓΗΘΟΥΝ;

TRO THERAPEUTIC RADIOLOGY AND ONCOLOGY
AN OPEN ACCESS JOURNAL COVERING ALL ASPECTS RELATED TO RADIATION AND ONCOLOGY

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Home / January 2019 / Stereotactic ablative radiation therapy for operable early-stage lung cancer—considerations and controversies

Review Article

Stereotactic ablative radiation therapy for operable early-stage lung cancer—considerations and controversies

Christopher P. Daniels¹, Drew Moghanak



Cancers (Basel). 2018 Sep; 10(9): 310.
Published online 2018 Sep 4. doi: [10.3390/cancers10090310](https://doi.org/10.3390/cancers10090310)

PMCID: P
PMID:

Surgical Resection Versus Stereotactic Body Radiation Therapy for Stage I NSCLC: Can Randomized Trials Provide the Solution?

[Melanie P. Subramanian](#) and [Bryan F. Meyers](#)*

September 2018

Stereotactic Body Radiation Therapy for Operable Early-Stage Lung Cancer

Findings From the NRG Oncology RTOG 0618 Trial

Robert D. Timmerman, MD^{1,2}; Rebecca Paulus, BS³; Harvey I. Pass, MD⁴; et al

SABR for Operable Patients

- JCOG 0403 (12 Gy x 4 fractions)
 - 3-yr OS=76% (95% CI: 63.2%–84.8%)
 - **3-yr LPFS = 68.5%** (95% CI: 55.5%–78.4%) (**86% LC**)
 - 8% Grade 3 toxicity (no grade 4-5 toxicity)
- RTOG 0618 (18Gy x 3 fractions)
 - **2-year LF, RF, and DF are 19.2%, 11.7%, and 15.4%, respectively.**
 - 2-year estimates of PFS and OS are 65.4% and 84.4%, respectively.
 - 16% Grade 3 toxicity
- Lagerwaard (n = 177, 40% > 3CM)
 - 177 pts (57% male, 40% > 3 cm)
 - **3-yr OS 84%, LC 93%**

ΑΝΑΓΚΗ ΤΥΧΑΙΟΠΟΙΗΜΕΝΩΝ ΜΕΛΕΤΩΝ

Surgical Resection Versus Stereotactic Body Radiation Therapy for Stage I NSCLC: Can Randomized Trials Provide the Solution?

Melanie P. Subramanian and Bryan F. Meyers*

ΑΝΑΓΚΗ ΤΥΧΑΙΟΠΟΙΗΜΕΝΩΝ ΜΕΛΕΤΩΝ

Randomized Trials Comparing Surgery to SBRT

ROSEL: Radiosurgery or Surgery
for operable stage I NSCLC



Cyber knife Trial (STARS)

- Randomized trial comparing surgery (lobectomy) to SBRT for Stage I NSCLC
- SBRT dose: 12.5 Gy x 4 fractions
- Cyberknife users only
- Multi-institutional
- PI: Jack Roth, M.D.
- Lobectomy candidates

ACOSOG Z4099/ROG 1021 Phase III Trial for High-risk patients Opened June 2011

Histological confirmation
NSCLC and
confirmation
N2/N3
negative
lymph nodes

Registration and
Randomization

ARM 1:
Sublobar
Resection ±
Brachytherapy
(SR)

ARM 2:
Stereotactic
Body Radiation
Therapy (SBRT)
18 Gy X 3 = 54
Gy

F
O
L
L
O
W
U
P

Endpoint: 3 year OS
Accrual = 420 patients

Operable Stage I NSCLC- SABR trials

Phase II

JCOG 0403	stage I, 65 pts	3yr LC 68.5%, 3yr OS 76%
RTOG 0618	stage I/II	Reported

Phase III

ROSEL	Stage IA Radiosurgery Or Surgery for operable Early stage NSCLC	close due to lack of accrual
STARS	Stage I Stereotactic Radiotherapy with Surgical resection	close due to lack of accrual
ACOSOG Z4099/ ROG 1021	Radiosurgery vs. Sublobar resection +/- brachytherapy	close due to lack of accrual

.....ΑΠΟ ROSEL KAI STARS

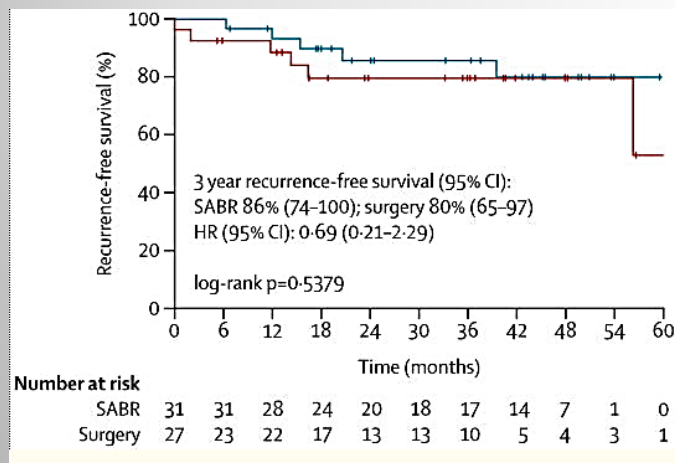
[Lancet Oncol. 2015 Jun; 16\(6\): 630–637.](#)

PMID: [25981812](#)

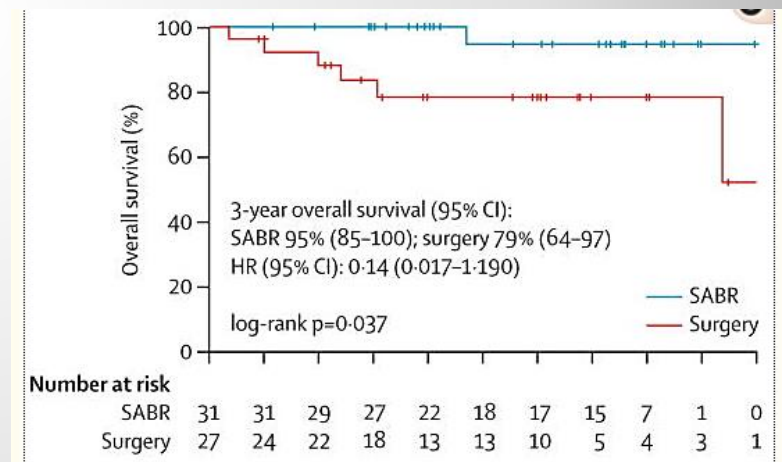
Published online 2015 May 13. doi: [10.1016/S1470-2045\(15\)70168-3](#)

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,[†] and Jack A Roth[†]



ΤΟΠΙΚΟΣ ΕΛΕΓΧΟΣ



ΕΠΙΒΙΩΣΗ

LANCET ONCOLOGY JUN 2015

ΌΜΩΣ.. ΠΕΡΙΣΣΟΤΕΡΕΣ ΟΙ ΤΟΠΙΚΟΠΕΡΙΟΧΙΚΕΣ ΥΠΟΤΡΟΠΕΣ ΜΕ SBRT

Analysis of First Recurrence and Survival in Patients with Stage I Non-Small Cell Lung Cancer Treated with Surgical Resection or Stereotactic Radiation Therapy

[Traves Crabtree](#), MD,¹ [Varun Puri](#), MD,¹ [Clifford Robinson](#), MD,³ [Jeffrey Bradley](#), MD,³ [Stephen Broderick](#), MD,¹ [G Alexander Patterson](#), MD,¹ [Jingxia Liu](#), PhD,² [Joanne F Musick](#), RN,¹ [Jennifer M Bell](#), BSN,¹ [Michael Yang](#), BS,¹ and [Bryan F Meyers](#), MD MPH¹

Total Proportion of Local, Regional, and Distant Recurrences Occurring in All Patients with Stage 1 NSCLC Treated with Surgery or SBRT

	NO Recurrence	Local Recurrence	Regional Recurrence	Distant Recurrence
Surgery	77.7%	2.6%	7.0%	12.7%
SBRT	66%	10.7%	10%	13.3%



• KATEΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ NCCN 2014

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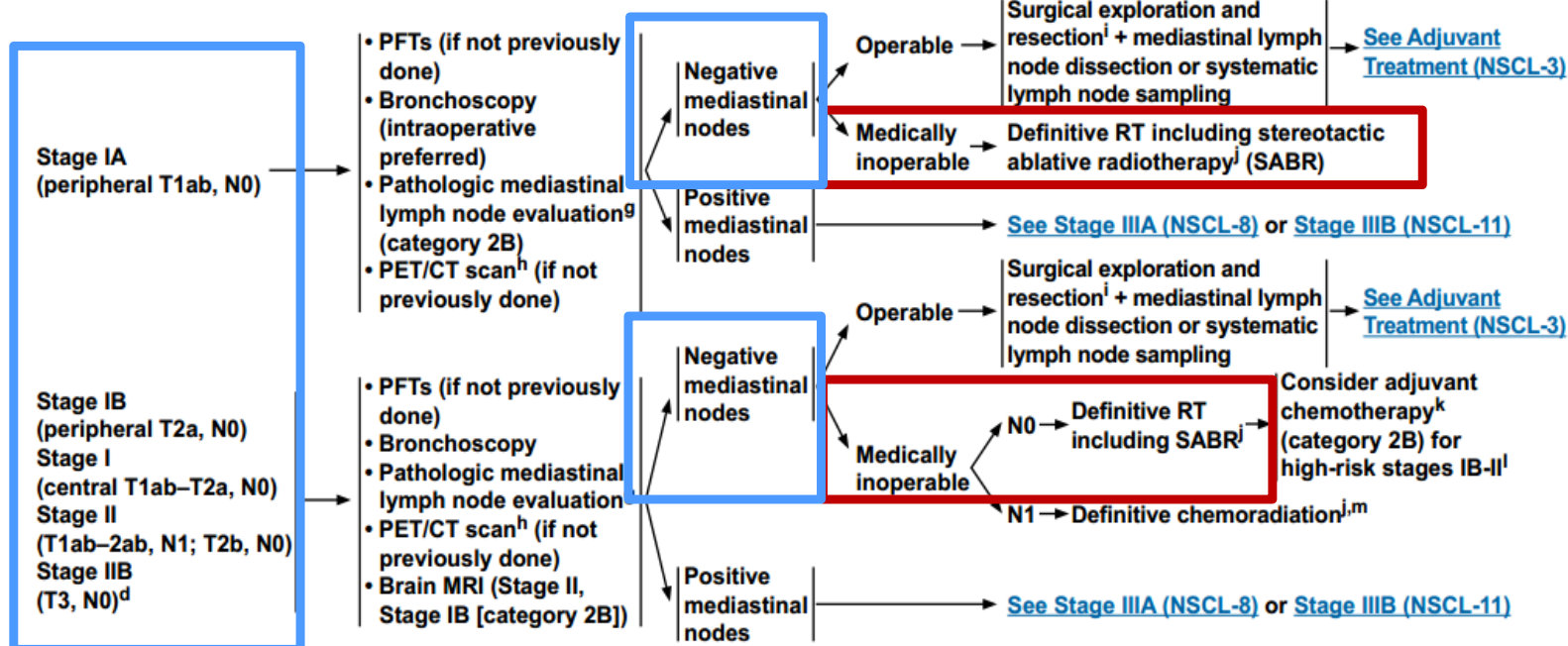
NCCN Guidelines Version 3.2014 Non-Small Cell Lung Cancer

[NCCN Guidelines Index](#)
[NSCLC Table of Contents](#)
[Discussion](#)

CLINICAL ASSESSMENT

PRETREATMENT EVALUATION^f

INITIAL TREATMENT



• ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ NCCN 2019

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NCCN Guidelines Version 4.2019 Non-Small Cell Lung Cancer

CLINICAL ASSESSMENT

PRETREATMENT EVALUATION^f

INITIAL TREATMENT

Stage IA
(peripheral T1ab, N0)

- PFTs (if not previously done)
- Bronchoscopy (intraoperative preferred)
- Pathologic mediastinal lymph node evaluation^g (category 2B)
- PET/CT scan^h (if not previously done)

Negative
mediastinal
nodes

Operable →

Surgical exploration and resectionⁱ + mediastinal lymph node dissection or systematic lymph node sampling

→ [See Adjuvant Treatment \(NSCL-3\)](#)

Medically inoperable →

Definitive RT including stereotactic ablative radiotherapy^j (SABR)

Positive
mediastinal
nodes

→ [See Stage IIIA \(NSCL-8\)](#) or [Stage IIIB \(NSCL-11\)](#)

Stage IB
(peripheral T2a, N0)
Stage I
(central T1ab–T2a, N0)
Stage II
(T1ab–2ab, N1; T2b, N0)
Stage IIB
(T3, N0)^d

- PFTs (if not previously done)
- Bronchoscopy
- Pathologic mediastinal lymph node evaluation^g
- PET/CT scan^h (if not previously done)
- Brain MRI (Stage II, Stage IB [category 2B])

Negative
mediastinal
nodes

Operable →

Surgical exploration and resectionⁱ + mediastinal lymph node dissection or systematic lymph node sampling

→ [See Adjuvant Treatment \(NSCL-3\)](#)

Medically inoperable →

N0 → Definitive RT including SABR^j

Consider adjuvant chemotherapy^k (category 2B) for high-risk stages IB-II^l

N1 → Definitive chemoradiation^{j,m}

Positive
mediastinal
nodes

→ [See Stage IIIA \(NSCL-8\)](#) or [Stage IIIB \(NSCL-11\)](#)

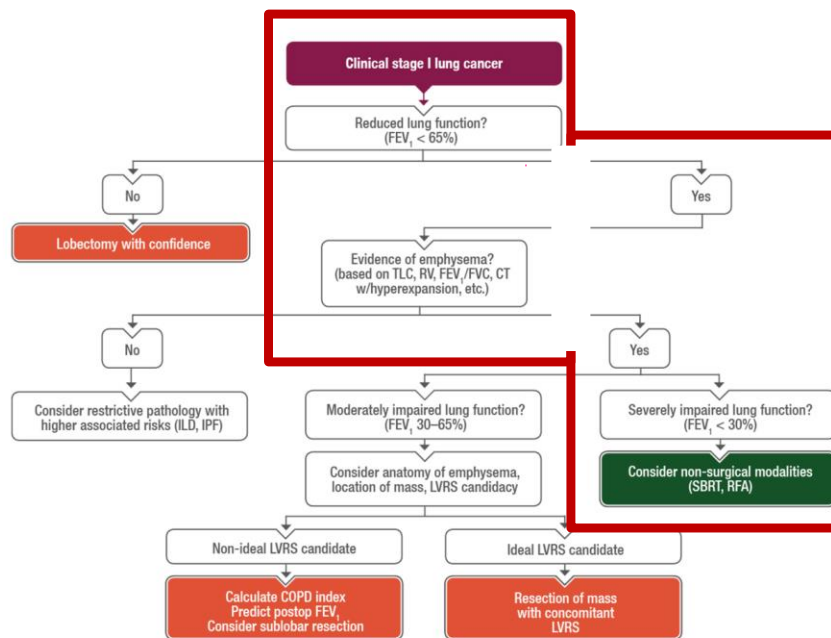
CLINICAL PRACTICE GUIDELINES

Staging and risk assessment

Patients with clinical stage I lung cancer and
limited pulmonary function due to emphysema

Yacoub WN et al. Semin Thorac Cardiovasc
Surg 2010;22:38–43.

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CLINICAL PRACTICE GUIDELINES

Treatment

Early NSCLC (stages I and II)
– Radiotherapy

Summary of recommendations

Primary radiotherapy	<u>SABR/SBRT in stage I is the treatment of choice at a biologically equivalent tumour dose of ≥ 100 Gy to the encompassing isodose</u>
	<u>SABR is associated with low toxicity in peripheral lung tumour in elderly and COPD patients</u>
	<u>Salvage surgery may be offered to patients with complications post-SABR</u>
	For medically inoperable <u>patients with tumours > 5 cm and/or moderately central location</u> , radical RT using more conventional or accelerated schedules is recommended

• ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ 2019

Draft
NICE
Guidance
2019

- For people with NSCLC who are well enough and for whom treatment with curative intent is suitable, offer lobectomy (either open or thoracoscopic). [2019]
- For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline lobectomy or in whom it is contraindicated, offer radical radiotherapy with stereotactic ablative radiotherapy (SABR) or sublobar resection. [2019]
- For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline surgery or in whom any surgery is contraindicated, offer SABR. If SABR is contraindicated, offer alternative radical radiotherapy. [2019]



ΣΑΣ ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ!!!