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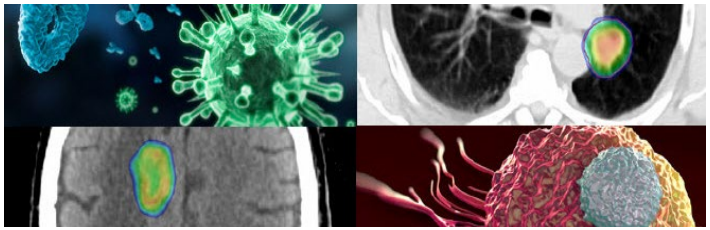


DKTK

DEGRO AG Stereotaxie

Lungtech-RETRO: SBRT for central lung tumors

Eleni Gkika, Sonja Adebahr, Ursula Nestle, Anca-L. Grosu
Department of Radiation Oncology
University Medical Center Freiburg

PROJEKT- OUTLINE: „LUNGTECH - RETRO“ - RATIONALE

Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located Non–Small-Cell Lung Cancer: NRG Oncology/RTOG 0813 Trial

Andrea Bezjak, MD[1]; Rebecca Paulus[2]; Laurie E. Gaspar, MD[3]; Robert D. Timmerman, MD[4]; William L. Straube, MS[5]; William F. Ryan, MD[6]; Yolanda I. Garces, MD[7]; Anthony T. Pu, MD[8]; Anurag K. Singh, MD[9]; Gregory M. Videtic, MD[10]; Ronald C. McGarry, MD, PhD[11]; Puneeth Iyengar, MD, PhD[4]; Jason R. Pantarotto, MD[12]; James J. Urbanic, MD[13]; Alexander Y. Sun, MD[1]; Megan E. Daly, MD[14]; Inga S. Grills, MD[15]; Paul Sperduto, MD[16]; Daniel P. Normolle, PhD[17]; Jeffrey D. Bradley, MD[5]; and Hak Choy, MD[4]

ORIGINAL ARTICLE

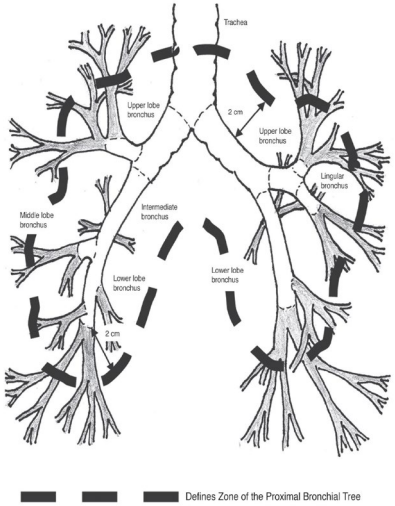
The HILUS-Trial—a Prospective Nordic Multicenter Phase 2 Study of Ultracentral Lung Tumors Treated With Stereotactic Body Radiotherapy

Karin Lindberg, MD, PhD,[a,b,*] Vitali Grozman, MD,[c,d] Kristin Karlsson, MSc, PhD,[a,e] Sara Lindberg, MD,[a,b] Ingmar Lax, MSc, PhD,[a,e] Peter Wersäll, MD, PhD,[a,f] Gitte Fredberg Persson, MD, PhD,[g,h,i] Mirjana Josipovic, MSc, PhD,[g] Azza Ahmed Khalil, MD, PhD,[j] Ditte Sloth Moeller, MSc, PhD,[j] Jan Nyman, MD, PhD,[k,l] Ninni Drugge, MSc, PhD,[m] Per Bergström, MD, PhD,[n] Jörgen Olofsson, MSc, PhD,[n] Lotte Victoria Rogg, MD, PhD,[o] Christina Ramberg, MSc, PhD,[p] Charlotte Kristiansen, MD, PhD,[q] Stefan Starup Jeppesen, MD, PhD,[r,s] Tine Bjørn Nielsen, MSc, PhD,[t] Britta Lödén, MD,[u] Hans-Olov Rosenbrand, MSc,[u] Silke Engelholm, MD, PhD,[v] André Haraldsson, MSc, PhD,[v] Charlotte Billiet, MD, PhD,[w,x] Rolf Lewensohn, MD, PhD[a,b]

- Recently published data of RTOG 0813 and the HILUS trial show that the safety and efficacy of SBRT in central tumors remains unclear.
- Data for evaluating **the tolerance of mediastinal structures** is of high interest.
- Single centre series are far too small to draw any conclusions, huge retrospective database analyses often lack important information.

EORTC 22113-8113 LUNGTECH-TRIAL

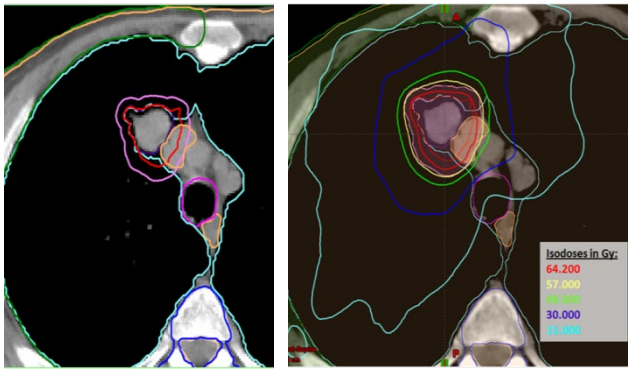
SBRT of central NSCLC: 8X 7.5Gy = 60Gy



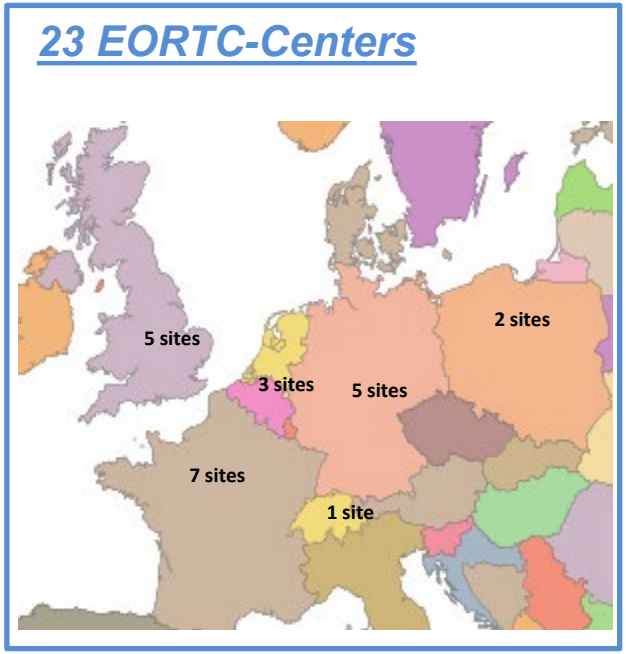
Timmerman et al , JCO 2006

Primary Endpoint:
Freedom of local progression rate at 3 years

Secondary Endpoints:
- Toxicity
- Pattern of recurrence
- Overall survival
- Causes of death



Modif. from Adebahr et al, BJR 2015



Central Review

Expert review: Staging

Expert review: Eligibility for RT

INCLUSION

- Centrally located NSCLC
- Non-metastatic
- medically inoperable
- Staging CT + FDG PET/CT
- Eligibility Criteria
- Informed Consent

Eligibility confirmation

RTQA Central Review: Delineation & Treatment planning

Treatment plan confirmation

4D-CT RT planning- using 3D FDG-PET/CT co-matching

IG-SBRT with CBCT verification: 8 X 7.5Gy = 60Gy

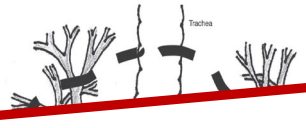
RTQA Central Review: Treatment verification CBCT

Follow up (FU): Local control (CT + PET-CT or biopsy if required)

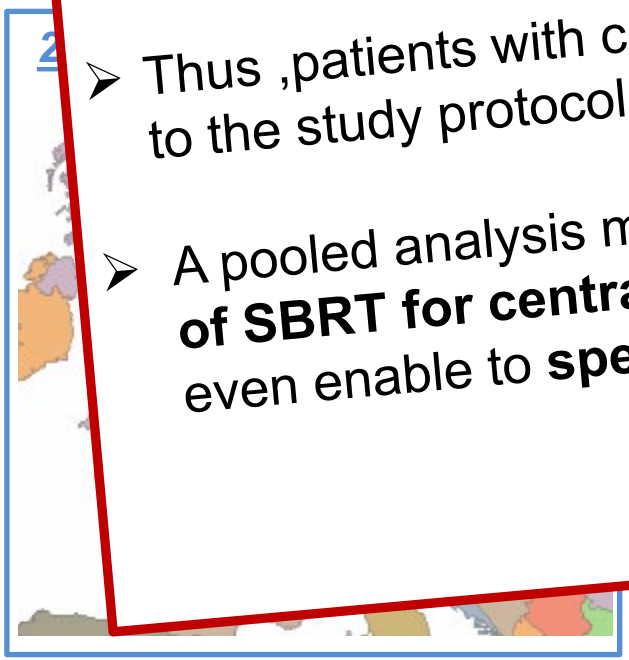
FU: 6 weeks after SBRT,
year 1-3: 3 monthly visits
year 4-5: 6 monthly
until end of the trial: yearly

EORTC 22113-8113 LUNGTECH-TRIAL

SBRT of central NSCLC: 8X 7.5Gy = 60Gy



- Between 08/15 and 12/17 inclusion of 39 pat.
- 2 stops of accrual due to strict stopping rules when potential “toxic deaths” had to be excluded
- Early stop of recruitment in 12/17 , ´Follow up ongoing
- Thus ,patients with central lung tumors have been treated in analogy to the study protocol or with some modified treatment schedules
- A pooled analysis might lead to further insights on **toxicity and safety of SBRT for central and “ultra-central” lung tumors** and might even enable to **specify dose-effect correlations**.



Consent

FU: 6 weeks after SBRT,
year 1-3: 3 monthly visits
year 4-5: 6 monthly
until end of the trial: yearly

PROJEKT- OUTLINE: „LUNGTECH - RETRO“

OBJECTIVE:

To establish a database of patients with **centrally and ultra-centrally located lung tumors** (**NSCLC** and **pulmonary metastases** of otherwise controlled primaries in 2 separate approaches) treated with **highly conformal, dose-escalated image-guided radiotherapy techniques** to retrospectively analyze **the toxicity and dose-effect correlations for mediastinal risk organs**, as well as **efficacy of SBRT** in these patients **.**

Primary endpoint:

- Acute and late toxicity

Secondary endpoint(s):

- Freedom from local progression at three years after start of SBRT
- Patterns of local and distant recurrence , local progression free survival
- Overall survival and cause of death
- Dose-effect correlations for mediastinal risk organs (subproject).

Endpoint analysis will be performed separately for NSCLC and pulmonary lesions.

PROJEKT- OUTLINE: „LUNGTECH - RETRO“

➢ Key Eligibility criteria for SBRT patients:

- Indication and performance of SBRT in patients with **centrally located** (defined as tumor within 2 cm or touching the zone of the proximal bronchial tree or tumor that is immediately adjacent to the mediastinal or pericardial pleura, with a PTV expected to touch or include the pleura mediastinal)
  early stage NSCLC OR pulmonary metastases of an otherwise controlled primary tumor.

- Lesions confirmed by either histology or cytology or clear imaging signs (CT-suspicion, growth, FDG uptake) of malignant tumors

- No previous radiation from the thorax and / or mediastinum

- No chemotherapy or targeted therapy within 3 months before SBRT onset.

- No other malignancies, except adequately treated basal cell carcinoma or other malignancies, of which the patient has been disease-free for at least 5 years. If there is histological confirmation of NSCLC, 2 years of malignancy are sufficient for inclusion.

- Patients must have received a Biologically Effective Dose (BED) of at least 50 Gy ($\alpha/\beta = 10$; minimum EQD-2 ≥ 41.7 Gy) with highly conformal, image-guided radiotherapy techniques

- Any fractionation <= 8 is acceptable, as long as the BED is 50 Gy or more (EQD-2 ≥ 41.7 Gy)

PROJEKT- OUTLINE: „LUNGTECH - RETRO“

To be done / discussed:

- PI will provide ethical approval (for the whole project), project plan, for each center the local P

- PI will send around an Excel database to collect data (within 4 months):
  - Baseline characteristics
  - SBRT data (RT and Dose-/volume information for OAR and for target volumes)
  - Outcome data: acute toxicity, late toxicity, LC, PFS, OS

- Analyses and drafting of manuscript
  All participating center are very welcome to participate in the analysis, review the results in detail and access the central database at the PIs center upon request and available schedules.

- Publication:
  All clinics providing data can name one co-author on each publication; clinics providing ten or more patients can name co-author on each publication.
  As based on the AG guidelines.
  For each project plan sub-analysis a publication may arise.

PROJEKT- OUTLINE: „LUNGTECH - RETRO“

- Eligibility criterion:
  Patients must have received a **Biologically Effective Dose (BED) of at least 50 Gy (α/β= 10; minimum EQD-2 ≥ 41.7 Gy)** with highly conformal, image-guided radiotherapy techniques.
  Any fractionation <= 8 is acceptable, as long as the BED is 50 Gy or more (EQD-2 ≥ 41.7 Gy) ,

- **Contact**: *eleni.gkika@uniklinik-freiburg.de*

PROJEKT- OUTLINE: „LUNGTECH - RETRO“

Diskussion/ Vorschläge aus Publikum:

- Dosis nicht begrenzen, bis 12 Fraktionen zulassen.
- Cut off hinsichtlich zeitlichem Einschluss definieren, modernes Kollektiv
- Bestrahlungsparameter von Beginn an detailliert erfassen
- Für Analyse der Pläne: Konturierung muss ohnehin durch PI kontrolliert werden,

  Nachkonturierungen erfolgen dann von dort aus einer Hand, für aktuell definierten

  Fragestellungen Freiburg
- Heidelberg, Würzburg und Zürich bekunden neben survey ebenfalls Interesse an Teilnahme

Herzlichen Dank

für Ihre Aufmerksamkeit!

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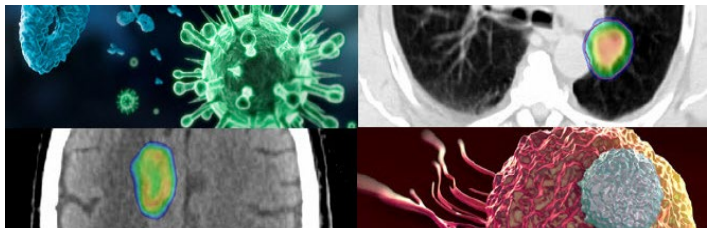

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