Role of Radiation therapy in Early stage Lung cancer

A.F.M. Kamal Uddin
MBBS, DTCD, MD
Consultant Radiation Oncology
Kamal1325@yahoo.com
Cancer Burden

As per GOLOBOCAN 2008

Total population : 160 million

- Five years Cancer survival prevalence : 291.2 thousand
- New Cases per year : 141.1 thousand
- Number of cancer death: 103.3 thousand
- New and Old cases : 124.8 thousand
Incidence

18,663 (31.1%)
5,048 (8.4%)
4,121 (6.9%)
3,392 (5.7%)
3,198 (5.3%)
2,859 (4.8%)
2,758 (4.6%)
2,736 (4.6%)
2,302 (3.8%)
14,951 (24.9%)

Legend:
- Lung
- Lip, oral cavity
- Oesophagus
- Other pharynx
- Stomach
- Non-Hodgkin lymphoma
- Larynx
- Colorectum
- Liver
- Other and unspecified
Estimated age-standardised incidence and mortality rates: both sexes

- Cervix uteri
- Breast
- Lung
- Lip, oral cavity
- Oesophagus
- Stomach
- Other pharynx
- Colorectum
- Ovary
- Liver
- Gallbladder
- Non-Hodgkin lymphoma
- Larynx
- Bladder
- Prostate

Legend:
- Incidence
- Mortality
Facts of Lung cancer

- Types:
  - Non Small Cell Lung Cancer (NSCLC) - 80%
  - Small Cell Lung Cancer (SCLC) - 20%
Management overview of SCLC
SCLC is a very chemo sensitive tumor with very poor prognosis.
Common believes:

- Chemotherapy is the prime modality of cancer treatment
- Chemo therapy is effective and cheaper
- ............
# Stage wise treatment recommendation for SCLC

<table>
<thead>
<tr>
<th>Stage</th>
<th>Recommended treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited</td>
<td>concurrent cisplatin and etoposide (4c every 3 weeks) with early RT during cycle 1 or 2 (45 Gy/1.5 Gy b.i.d. preferred). If CR or near-CR, prophylactic cranial RT (25 Gy in 10 fx) For &lt;5% of patients with cT1-2No disease with negative mediastinoscopy (or endoscopic biopsy), lobectomy and mediastinal node dissection/sampling may be performed initially. If pN0, chemotherapy along. If pN+, concurrent chemoradiation as above</td>
<td>MS 20 months, 5-year OS 20–26%</td>
</tr>
<tr>
<td>Extensive</td>
<td>Combination platinum-based chemotherapy ± palliative RT to symptomatic sites. For patients with PR or CR to chemotherapy, consider prophylactic cranial RT (25 Gy in 10 fx). If brain metastases present, WBRT (30–37.5 Gy in 10–15 fx)</td>
<td>MS 12 months, 5-year OS &lt;5–10%</td>
</tr>
</tbody>
</table>
Land mark trial on SCLC

TWICE-DAILY COMPARED WITH ONCE-DAILY THORACIC RADIOTHERAPY IN LIMITED SMALL-CELL LUNG CANCER TREATED CONCURRENTLY WITH CISPLATIN AND ETOPOSIDE

ANDREW T. TURRISI, III, M.D., KYUNGMAH KIM, Ph.D., RONALD BLUM, M.D., WILLIAM T. SAUSE, M.D., ROBERT B. LIVINGSTON, M.D., RITSUKO KOMAKI, M.D., HENRY WAGNER, M.D., SEENA AISNER, M.D., AND DAVID H. JOHNSON, M.D.
Turrisi - Methods

- 419 pts (’89-’92) with LS-SCLC
- Concurrent Chemo x4c (cis/etopo) q3w
- Radiation
  - Group 1: 1.8 Gy QD to 45 Gy
  - Group 2: 1.5 Gy BID to 45 Gy
- Bilateral mediastinal and ipsilateral hilar adenopathy
- Prophylactic Cranial Irradiation if CR
  - 25 Gy/ 10 fx
## Turrisi – Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>2-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily</td>
<td>41%</td>
<td>16%</td>
</tr>
<tr>
<td>Twice-daily</td>
<td>47%</td>
<td>26%</td>
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</tbody>
</table>

$P = 0.04$
Management overview of NSCLC
Presentation by Stage

- Stage I 10%
- Stage II 20%
- Stage III 30%
- Stage IV 40%
Surgery

- Best chance for cure for tumors limited to hemithorax
- Controversial about the MGMT of N2
  - Preop detection: <10% 5yr
  - Occult detection: 30% 5yr
- N3/T4 is considered inoperable by most.
- Solitary mets: “has been success in removing the primary tumor as well as a solitary metastatic focus”
Radiation Therapy

- Primary modality for cure in unresectable disease.
- Maximum dose: yet to be established
  - Standard 60-65Gy
    - W/O Chemo: LC 15%
      - “higher doses appear to be required for improved local control”
    - Doses as high as 102.9 Gy for small and 81Gy for large tumors have been delivered safely.
Chemotherapy

- **Single Tx for wet IIIB-IV**
  - Prolongs MS and improves Sx/QOL compared to “best supportive care”

- **Used in conjuction w/ XRT for LAD**
  - Neoadjuvant (Dillman)
  - Concurrent (Japanese, RTOG 9410)

- **Adjuvant to RXN for IB-IIIA**
  - IALT (International Adjuvant Lung cancer Trial)
  - ?ALPI
PRINCIPLES OF RADIATION THERAPY (1 of 9)

General Principles (see Table 1. Commonly Used Abbreviations in Radiation Therapy)

- Determination of the appropriateness of radiation therapy (RT) should be made by board-certified radiation oncologists who perform lung cancer RT as a prominent part of their practice.
- RT has a potential role in all stages of NSCLC, as either definitive or palliative therapy. Radiation oncology input as part of a multidisciplinary evaluation or discussion should be provided for all patients with NSCLC.
- The critical goals of modern RT are to maximize tumor control and to minimize treatment toxicity. A minimum technologic standard is CT-planned 3D-CRT.¹
- More advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) 4D-CT and/or PET-CT simulation, IMRT/VMAT, IGRT, motion management, and proton therapy. Nonrandomized comparisons of using advanced technologies versus older techniques demonstrate reduced toxicity and improved survival.²,⁴
- Centers using advanced technologies should implement and document modality-specific quality assurance measures. The ideal is external credentialing of both treatment planning and delivery such as required for participation in RTOG clinical trials employing advanced technologies. Useful references include the ACR-ASTRO Practice Guidelines for Radiation Oncology (http://www.acr.org~/media/ACR/Documents/PGTS/toc.pdf).

Early-Stage NSCLC (Stage I)

- SABR (also known as SBRT) is recommended for patients who are medically inoperable and who refuse to have surgery after thoracic surgery evaluation. SABR has achieved primary tumor control rates and overall survival, comparable to lobectomy and higher than 3D-CRT in nonrandomized and population-based comparisons in medically inoperable or older patients.⁶-¹⁰
- SABR is also an appropriate option for patients with high surgical risk (able to tolerate sublobar resection but not lobectomy, e.g., ≥ age 75 years, poor lung function). SABR and sublobar resection achieve comparable cancer-specific survival and primary tumor control.¹⁰-¹²
- For institutions without an established SABR program, more modestly hypofractionated or dose-intensified conventionally fractionated 3D-CRT regimens are alternatives.¹³-¹⁴
- In patients treated with surgery, postoperative radiotherapy (PORT) is not recommended unless there are positive margins or upstaging to N2 (see Locally Advanced NSCLC below).

Locally Advanced NSCLC (Stage II-III)

- The standard of care for patients with inoperable stage II and stage III is concurrent chemoRT.¹⁶-¹⁷ (http://www.acr.org~/media/ACR/Documents/AppCriteria/Oncology/NonsurgicalTreatmentForNSCLCGoodPerformanceStatusDefinitiveIntent.pdf) RT interruptions and dose reductions for manageable acute toxicities should be avoided by employing supportive care.
- Sequential chemoRT or RT alone is appropriate for frail patients unable to tolerate concurrent therapy.¹⁸,¹⁸ (http://www.acr.org~/media/ACR/Documents/AppCriteria/Oncology/NonsurgicalTreatmentForNSCLCPoorPerformanceStatusOrPalliativeIntent.pdf)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Locally Advanced NSCLC (Stage II-III) (continued)

• Accelerated RT regimens may be beneficial, particularly if not concurrent with chemotherapy (i.e., in a sequential or RT-only approach). 20,21
• RT has a role before or after surgery.
  
  [link: http://www.acr.org~/media/ACR/Documents/AppCriteria/Oncology/InductionAndAdjuvantTherapyFor2NSCLC.pdf]
  
  ▶ Preoperative concurrent chemoRT is an option for patients with resectable stage IIIA (minimal N2 and treatable with lobectomy) 22 and is recommended for resectable superior sulcus tumors. 23-24
  
  ▶ Preoperative chemotherapy and postoperative RT is an alternative for patients with resectable stage IIIA. 25,28
  
  ▶ The determination of resectability in trimodality therapy should be made prior to initiation of all treatment.
  
  ▶ In patients with clinical stage IV upstaged surgically to N2+, PORT appears to improve survival significantly as an adjunct to postoperative chemotherapy in non-randomized analyses. 27,28 Although the optimal sequence is not established, PORT is generally administered after postoperative chemotherapy. PORT with concurrent chemotherapy can be administered safely in medically fit patients 29-31 and is recommended for positive resection margins.
  
  ▶ PORT is not recommended for patients with pathologic stage N0-1 disease, because it has been associated with increased mortality, at least when using older RT techniques. 32

Advanced/Metastatic NSCLC (Stage IV)

• RT is recommended for local palliation or prevention of symptoms (such as pain, bleeding, or obstruction).
• Definitive local therapy to isolated or limited metastatic sites (oligometastases) (including but not limited to brain, lung, and adrenal gland) achieves prolonged survival in a small proportion of well-selected patients with good performance status who have also received radical therapy to the intrathoracic disease. Definitive RT to oligometastases, particularly SABR, is an appropriate option in such cases if it can be delivered safely to the involved sites. 33-36
• See the NCCN Guidelines for Central Nervous System Cancers regarding RT for brain metastases.

Target Volumes, Prescription Doses, and Normal Tissue Dose Constraints (See Tables 2-5 on NSCLC-C 6 of 9 and NSCLC-C 7 of 9)

• ICRU Reports 62 and 83 detail the current definitions of target volumes for 3D-RT and IMRT. GTV comprises the known extent of disease (primary and nodal) on imaging and pathologic assessment, CTV includes regions of presumed microscopic extent or dissemination, and PTV comprises the ITV (which includes margin for target motion) plus a setup margin for positioning and mechanical variability.
  
  [link: http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx]
  
  ▶ PTW margin can be decreased by immobilization, motion management, and IGRT techniques.
  
  ▶ Consistent delineation of normal structures is critical for evaluating plans for safety. The RTOG consensus lung-contouring atlas is a useful resource. [link: http://www.rtog.org/CoreLab/ContouringAtlases/LungAtlas.aspx]
  
  ▶ Commonly used prescription doses and normal tissue dose constraints are summarized in Tables 2-5. These are based on published experience, ongoing trials, historical data, modeling, and empirical judgment. 37,38 Useful references include the recent reviews of normal organ dose responses from the QUANTEC project. 39-43

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Treatment Summary

- **Stage –I-II**: Surgery followed by Adjuvant chemo Platinum based 4 cycles, Adjuvant Radiation if margin positive.
- **Stage- I&II** (In-operable), IIIA, IIIB (dry)-Concurrent Chemo and Radiation therapy with minimum 66 GY
- **Stage-IIIB** (with pleural effusion) and **Stage-IV**- Palliative chemotherapy with palliative radiation therapy when required.

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Pathologic stage</th>
<th>Clinical stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1,N0,M0</td>
<td>67%</td>
<td>61%</td>
</tr>
<tr>
<td>IB</td>
<td>T2,N0,M0</td>
<td>57%</td>
<td>38%</td>
</tr>
<tr>
<td>IIA</td>
<td>T1,N1,M0</td>
<td>55%</td>
<td>34%</td>
</tr>
<tr>
<td>IIB</td>
<td>T2,N1,M0</td>
<td>39%</td>
<td>24%</td>
</tr>
<tr>
<td>IIB</td>
<td>T3,N0,M0</td>
<td>38%</td>
<td>22%</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3,N1,M0</td>
<td>25%</td>
<td>9%</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-3,N2,M0</td>
<td>23%</td>
<td>13%</td>
</tr>
</tbody>
</table>
Treatment for early stage lung cancer

- Mostly it was surgery
- Radiation for those who were not fit for surgery
"THE TREATMENT OF CARCINOMA OF THE BRONCHUS A Clinical Trial to Compare Surgery and Super voltage Radiotherapy"
(Morrison R, Lancet. 1963)

- Randomized. 58 patients,
- Arm 1:
  - RT - using 8 MeV linac, 45 Gy in 4 weeks daily. Target + 2cm + hilar/mediastinal areas
- Arm 2:
  - Surgery - pneumonectomy or lobectomy + hilar/mediastinal LND.
- 13/30 weren't operable/refused.
- Histology squamous 64%, adenocarcinoma 3%, small cell/anaplastic 33%
Outcome:

- **1-year OS**
  - RT 64% vs. Surgery 43%;

- **2-year OS**
  - 14% vs. 27%;

- **4-year**
  - 7% vs. 23% (NS).

- **By histology:**
  - squamous 6% vs. 30% (SS);
  - small cell 10% both (NS)

- **Conclusion:**
  - In squamous cell tumors, surgical resection is significantly better than RT; no difference in small cell.
Conventional RT treatment

- Retrospective.
- N=200 Stage I NSCLC
- Arm 1: RT alone. 2D planning (n=115),
- Arm 2: 3D planning (n=85).
- Median RT dose 64 Gy vs. 66 Gy (NS).
- Age 69 vs 73 (SS).
- Median F/U 1.7 years vs. 1.6 years (NS).
- Outcome: 5-year OS 2D 10% vs. 3D 36% (SS);
  5-year LC 34% vs. 70% (SS).
Dose escalation

- Memorial Sloan Kettering: 2007
- Retrospective. 82 patients, inoperable NSCLC Stage I-IIIB (I-II n=55; III n=27).
- Dose $\geq 80$ Gy using 3D-CRT with sequential chemotherapy
- 5-year Outcome:
  - Stage I/II LC 67%, OS 36%, median OS 3.4 years
  - Stage III LC 39%, OS 31%, median OS 2.7 years
Newer techniques of RT

• SBRT-Stereotactic Body RT

OR

• SABR-Stereotactic Ablative RT
SBRT Definition

- A technique used to deliver
- High, ablative doses limited
- In a number (1-5) of fractions
- To extra cranial target
Features of SBRT

- Meticulous immobilization
- Accurate repositioning
- Minimization of normal tissue exposure by using multiple fields (like 3D CRT or IMRT)
- Rigorous accounting of organ and target motion
- Stereotactic registration with fiducial markers or surrogates of tumor targets and normal tissue avoidance structures
- Ablative dose fractionation with sub-centimeter accuracy
4-Dimensional Radiation Therapy
Treatment for the New Millennium—the addition of the TIME dimension
Techniques for Motion Control

- Abdominal compression - limit respiratory motion from the diaphragm
- Respiratory gating - beam on only during a specific phase of respiration
- Respiratory tracking - move the beam to follow the target
STEREOTACTIC BODY RADIATION THERAPY OF EARLY-STAGE NON-SMALL-CELL LUNG CARCINOMA: PHASE I STUDY

RONALD C. McGARRY, M.D., Ph.D.,* LECH PAPIEZ, Ph.D.,* MARK WILLIAMS, M.D.,† TIA WHITFORD, R.N.,* AND ROBERT D. TIMMERMAN, M.D.‡

*Department of Radiation Oncology, Indiana University, Indianapolis, IN; †Pulmonary Division, Richard L. Roudebush VA Medical Center, Indianapolis, IN; ‡Department of Radiation Oncology, University of Texas Southwestern, Dallas, TX

Purpose: A Phase I dose escalation study of stereotactic body radiation therapy to assess toxicity and local control rates for patients with medically inoperable Stage I lung cancer.

Methods and Materials: All patients had non–small-cell lung carcinoma, Stage T1a or T1b N0, M0. Patients were immobilized in a stereotactic body frame and treated in escalating doses of radiotherapy beginning at 24 Gy total (3 × 8 Gy fractions) using 7–10 beams. Cohorts were dose escalated by 6.0 Gy total with appropriate observation periods.

Results: The maximum tolerated dose was not achieved in the T1 stratum (maximum dose = 60 Gy), but within the T2 stratum, the maximum tolerated dose was realized at 72 Gy for tumors larger than 5 cm. Dose-limiting toxicity included predominantly bronchitis, pericardial effusion, hypoxia, and pneumonitis. Local failure occurred in 4/19 T1 and 6/28 T2 patients. Nine local failures occurred at doses ≤16 Gy and only 1 at higher doses. Local failures occurred between 3 and 31 months from treatment. Within the T1 group, 5 patients had distant or regional recurrence as an isolated event, whereas 3 patients had both distant and regional recurrence. Within the T2 group, 2 patients had solitary regional recurrences, and the 4 patients who failed distantly also failed regionally.

Conclusions: Stereotactic body radiation therapy seems to be a safe, effective means of treating early-stage lung cancer in medically inoperable patients. Excellent local control was achieved at higher dose cohorts with apparent dose-limiting toxicities in patients with larger tumors. © 2005 Elsevier Inc.
SBRT Lung

- Timmerman phase I
- 47 pts medically inoperable lung cancer
- 8 Gy x 3 up to 24 Gy x 3
- T1 & T2 <5cm no MTD
- T2 >5cm MTD 66 Gy in 3 fractions
- DLT pneumonitis, pericardial effusion
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, Ramzi Abdulrahman, Colleen DesRosiers, Mark Williams, and James Fletcher

Abstract

Purpose
Surgical resection is standard therapy in stage I non-small-cell lung cancer (NSCLC); however, many patients are inoperable due to comorbid diseases. Building on a previously reported phase I trial, we carried out a prospective phase II trial using stereotactic body radiation therapy (SBRT) in this population.

Patients and Methods
Eligible patients included clinically staged T1 or T2 (≤ 7 cm), N0, M0, biopsy-confirmed NSCLC. All patients had comorbid medical problems that precluded lobectomy. SBRT treatment dose was 60 to 66 Gy total in three fractions during 1 to 2 weeks.

Results
All 70 patients enrolled completed therapy as planned and median follow-up was 17.5 months. The 3-month major response rate was 60%. Kaplan-Meier local control at 2 years was 95%. Altogether, 28 patients have died as a result of cancer (n = 5), treatment (n = 6), or comorbid illnesses (n = 17). Median overall survival was 32.6 months and 2-year overall survival was 54.7%. Grade 3 to 5 toxicity occurred in a total of 14 patients. Among patients experiencing toxicity, the median time to observation was 10.5 months. Patients treated for tumors in the peripheral lung had 2-year freedom from severe toxicity of 83% compared with only 54% for patients with central tumors.

Conclusion
High rates of local control are achieved with this SBRT regimen in medically inoperable patients with stage I NSCLC. Both local recurrence and toxicity occur late after this treatment. This regimen should not be used for patients with tumors near the central airways due to excessive toxicity.

J Clin Oncol 24:4833-4839. © 2006 by American Society of Clinical Oncology
SBRT Lung

- Timmerman phase II study of SBRT in medically inoperable stage I lung cancer
- 70 patients
- 60-66 Gy in 3 fractions
- 2 year local control 95%
- 2 year overall survival 56%
Timmerman

- Toxicity grade 3 or 4 - 8 patients
- Decreased PFT’s, pneumonia, pleural effusion, apnea, dermatitis
- 6 deaths - 4 pneumonia, 1 pericardial effusion, 1 massive hemoptysis (tumor vs tx)
UPMC Protocol

- Stereotactic radiation therapy for early stage lung cancer
- 60 Gy in 3 fractions for peripheral tumors
- 48 Gy in 4 fractions for central tumors
20 Gy x 3 Fractions = 60 Gy
Benefits of SBRT in Lung Cancer

- **SBRT**
  - 3-4 fractions
  - 1-2 weeks
  - Preservation of normal lung tissue & function
  - Much higher dose
  - Higher local control 80-95%
  - Cost >/=  

- **External Beam**
  - 35 fractions
  - 7 weeks
  - Fibrosis of more normal lung tissue
  - Lower dose
  - Local control 30-70%
SBRT: NOT

- Miracle when no other therapy left
- Big tumors
- Multiple tumors
- Spine mets without prior external beam RT
- Tumors invading the bowel, esophagus, etc
Patient selection: RTOG

- Age ≥18 years old
- Zubrod performance status 0 (fully active, unrestricted), 1 (restricted activities but able to work), or 2 (cares for self but unable to work).
- Cytologic or histologic proof of non-small cell cancer was required for entry.
- AJCC stages T1, T2 (≤5 cm), or T3 (≤5 cm peripheral tumors only), No, Mo cancer
- Based on both mandatory computed tomography (CT) and positron emission tomography (PET) screening.
Summary

- Benefits of SBRT for patients:
- FAST
- SAFE
- EFFECTIVE
- Ability to retreat when cannot give more external beam RT
- Minimal toxicity
- Cost often comparable
SABR disseminates rapidly

Pan et al, Cancer 2011;117(19):4566–72
Common SABR’ed cancer
Pan et al, Cancer 2011;117(19):4566–72
Why SABR became popular?

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Conv. EBRT</th>
<th>SABR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>60 Gy/30 Fx’s</td>
<td>48-54 Gy/3-4 Fx’s</td>
</tr>
<tr>
<td>LC, 90%</td>
<td>LC, 30%</td>
<td>LC, 90%</td>
</tr>
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Table 1. Results of various clinical trials of stereotactic body radiation therapy for lung cancer

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total dose (Gy)</th>
<th>Daily dose (Gy)</th>
<th>Reference point</th>
<th>Local control n (%)</th>
<th>Median follow-up (mo)</th>
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<tbody>
<tr>
<td>Uematsu et al. (2001) [5]</td>
<td>50-60</td>
<td>10</td>
<td>80% Margin</td>
<td>47/50 (94)</td>
<td>36</td>
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<tr>
<td>Arimoto et al. (1998) [8]</td>
<td>60</td>
<td>7.5</td>
<td>Isocenter</td>
<td>22/24 (92)</td>
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<tr>
<td>Timmerman et al. (2010) [9]</td>
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<td>18</td>
<td>80% Margin</td>
<td>54/55 (98)</td>
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<tr>
<td>Onimaru et al. (2003) [7]</td>
<td>48-60</td>
<td>6-7.5</td>
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<td>20/25 (80)</td>
<td>17</td>
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<td>Wulf et al. (2004) [10]</td>
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<td>15-15.4</td>
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<td>19/20 (95)</td>
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<td>Nagata et al. (2005) [6]</td>
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<td>12</td>
<td>Isocenter</td>
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<td>Xia et al. (2006) [11]</td>
<td>70 (50)</td>
<td>7 (5)</td>
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<td>41/43 (95)</td>
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<td>Baumann et al. (2009) [12]</td>
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<td>15</td>
<td>67% Margin</td>
<td>53/57 (92)</td>
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## SABR prospective trials
**medically inoperable lung cancer** -

<table>
<thead>
<tr>
<th>Study</th>
<th>No</th>
<th>RT dose</th>
<th>FU (mo)</th>
<th>LC (%)</th>
<th>OS (%)</th>
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<tbody>
<tr>
<td>Kyoto</td>
<td>45</td>
<td>12Gy x 4</td>
<td>32</td>
<td>94</td>
<td>83 (3-yr)</td>
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<tr>
<td>Indiana</td>
<td>70</td>
<td>20-22Gy x 3</td>
<td>50</td>
<td>92</td>
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<tr>
<td>Torino</td>
<td>62</td>
<td>15Gy x 3</td>
<td>28</td>
<td>88</td>
<td>57 (3-yr)</td>
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<tr>
<td>Scandinavian</td>
<td>57</td>
<td>15Gy x 3</td>
<td>35</td>
<td>92</td>
<td>60 (3-yr)</td>
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<tr>
<td>VU univ.</td>
<td>206</td>
<td>20Gy x 3 12Gy x 5 7.5Gy x 8</td>
<td>12</td>
<td>97</td>
<td>64 (2-yr)</td>
</tr>
</tbody>
</table>

88-97 at 3 yrs 56-83 at 3 yrs
Impact of Introducing Stereotactic Lung Radiotherapy for Elderly Patients With Stage I Non–Small-Cell Lung Cancer: A Population-Based Time-Trend Analysis

David Palma, Otto Visser, Frank J. Lagerwaard, Jose Belderbos, Ben J. Slotman, and Suresh Senan

ABSTRACT

Purpose
Stereotactic body radiotherapy (SBRT) for stage I non–small-cell lung cancer (NSCLC) is associated with high local control rates. The impact of introducing SBRT in patients 75 years of age or older was studied using a population-based cancer registry.

Methods
The Amsterdam Cancer Registry was assessed in three eras: 1999 to 2001 (period A, pre-SBRT); 2002 to 2004 (period B, some availability of SBRT), and 2005 to 2007 (period C, full access to SBRT). $\chi^2$, Kaplan-Meier, and Cox regression were used to compare treatment patterns and overall survival (OS) in three treatment groups: surgery, radiotherapy (RT), or neither.

Results
A total of 875 elderly patients were diagnosed with stage I NSCLC in the study period. Median follow-up was 54 months. Primary treatment was surgery in 299 patients (34%), RT in 299 patients (34%), and neither in 277 patients (32%). RT use increased between periods A and C (26% v 42%, $P < .01$), corresponding to a decrease in untreated patients. The percentage of RT patients undergoing SBRT in periods B and C was 23% and 55%, respectively. Median survival for all patients increased from 16 months in period A to 21 months in period C (log-rank $P < .01$; hazard ratio [HR] = 0.65; 95% CI, 0.54 to 0.80). The improvement in OS was confined to RT patients (HR = 0.70; 95% CI, 0.49 to 0.99), whereas no significant survival improvements were seen in the other groups.

Conclusion
SBRT introduction was associated with a 16% absolute increase in RT use, a decline in the proportion of untreated elderly patients, and an improvement in OS.

Introduction of lung SABR has led to an increased utilization of radiotherapy, a reduction in the proportion of untreated patients.
SABR in Elderly

- SBRT introduction was associated with a 16% absolute increase in RT use,
- a decline in the proportion of untreated elderly patients,
- an improvement in OS.
Slow dose CT decrease mortality of lung cancer
Case –SBRT Lung

- 76 yo with severe COPD
- 2003 wedge resection non small cell lung cancer
- PET CT 1/05 1.3 cm nodule RUL, PET +
- Not surgical candidate
Case-SBRT Lung

- 85 yo multiple medical problems
- 2.5 cm non small cell carcinoma in the right lower lobe
- Declined surgery
- CyberKnife 20 Gy x 3 fractions= total dose 60 Gy
Before                After
<table>
<thead>
<tr>
<th>Study</th>
<th>Stage/Fraction</th>
<th>Type/Medium</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>JCOG 0403</td>
<td>Stage I, 65 pts</td>
<td>3yr LC 68.5%, 3yr OS 76%</td>
<td></td>
</tr>
<tr>
<td>RTOG 0618</td>
<td>Stage I/II</td>
<td>will be reported</td>
<td></td>
</tr>
<tr>
<td>ROSEL</td>
<td>Stage IA</td>
<td>Radio surgery Or Surgery for operable Early stage NSCLC</td>
<td>close due to lack of accrual</td>
</tr>
<tr>
<td>STARS</td>
<td>Stage I</td>
<td>Stereotactic Radiotherapy with Surgical resection</td>
<td>close due to lack of accrual</td>
</tr>
<tr>
<td>ACOSOG Z4099/</td>
<td>Radiotherapy vs. Sublobar resection +/- brachytherapy</td>
<td>close due to lack of accrual</td>
<td></td>
</tr>
<tr>
<td>RTOG 1021</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Any less aggressive approach?
### SBRT for inoperable stage I NSCLC clinical results (retrospective)

<table>
<thead>
<tr>
<th>Author</th>
<th>Pt.no</th>
<th>Dose (Gy) / fr</th>
<th>3y-overall survival rate</th>
<th>Local control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uematsu (2001)</td>
<td>50</td>
<td>50-60Gy / 5-10fr</td>
<td>66%</td>
<td>94%</td>
</tr>
<tr>
<td>Hof (2003)</td>
<td>10</td>
<td>19-26Gy/ 1 fr</td>
<td>37%</td>
<td>60%</td>
</tr>
<tr>
<td>Onishi (2004)</td>
<td>26</td>
<td>72Gy/10 fr</td>
<td>64%</td>
<td>92%</td>
</tr>
<tr>
<td>Nagata (2005)</td>
<td>42</td>
<td>48Gy/4fr</td>
<td>IA 83%</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IB 72%</td>
<td></td>
</tr>
<tr>
<td>Onimaru (2008)</td>
<td>28</td>
<td>36-48Gy/4fr</td>
<td>IA 82%</td>
<td>64%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IB 32%</td>
<td></td>
</tr>
<tr>
<td>Takeda (2009)</td>
<td>63</td>
<td>50Gy/5fr</td>
<td>IA 90%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IB 63%</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

- **SBRT effective for operable stage I NSCLC.**
- **Encouraging option for elderly patients.**
- **Optimum treatment method will be developed in future**
- **Concurrent novel agents/chemo could be trued later.**
- **Newer machines and equipment will bring newer techniques which will bring bigger shift in the treatment pattern.**
United Hospital Experience

- 2 Cases of Metastatic lung
- 1 Case of HCC
Take Home Message

- Limited stage SCLC patient can achieve $\geq 25\%$ 5 years survival
- Early Stage NSLC is a curable disease with Radiation
- Only Radiation therapy by SABR is an option for curative treatment in Early stage NSCLC
- Old Age and other co-morbidities are not a barrier for SABR in NSCLC
- SABR in Early stage NSCLC is possible in Bangladesh.
Secret of Success: Combination of Seniors and Junior
Cancer-Multidisciplinary approach
Meet my future Tahmid and Fabiha...
We should work hard for a better future of the cancer patients!!