Stereotactic radiosurgery for operable lung cancer

Con

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Specific topics

• discuss the role of surgical treatment for early stage lung cancer
• determine important factors for long-term survival
• develop treatment algorithm for “small” lung cancers
• list major concerns when applying stereotactic radiotherapy (radiosurgery) to operable lesions
Against SRT in operable tumors

- surgical treatment for stage I lung cancer
  - complete resection: definition
  - lymph node staging
  - limited resection

- stereotactic radiotherapy as new treatment modality
  - how to obtain a pathological diagnosis?
  - how to determine nodal staging?
  - how to evaluate response and local recurrence rate?
  - how to select patients for adjuvant therapy?
  - radiotherapy issues
Against SRT in operable tumors

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SURGICAL THERAPY

• very effective therapy for early stage lung cancer
  *no large randomized studies*

• only applicable in 1/4 of cases

• resectability:
  – stage: clinical, surgical
  – medical status: respiratory, cardiac

• final aim = complete resection
COMPLETE RESECTION

depending on $R = \text{residual disease}$

- **R0** no residual tumor
- **R1** microscopic residual tumor
- **R2** macroscopic residual tumor
- **R** uncertain (to be tested prospectively)

Rami-Porta R et al. Lung Cancer 2005; 49:25
Complete resection (R0)

- Free resection margins proved microscopically
- Systematic or lobe-specific systematic nodal dissection:
  \[ \geq 6 \text{ nodes (3 mediastinal)} \]
- No extracapsular extension in nodes removed separately or at the margin of the lung specimen
- Highest mediastinal lymph node must be negative

Rami-Porta R et al. Lung Cancer 2005; 49:25
Lymph node staging

When there are no distant metastases lymph node involvement will determine prognosis!

Peroperative staging utmost important!

Meta-analysis: lymph node dissection ↑ survival

Wright G. Thorax 2006; 61:597
Rusch VW. J Thorac Oncol 2009; 4:568
Systematic nodal dissection

- dissection of mediastinal, hilar and lobar LN in a systematic fashion
- 240 pts cT1-3 N0-1 NSCLC
- 3 % expl. thoracotomy - 20 % N2 disease
- skip metastases : 34 % N2 disease
- no subgroup 0 % incidence of N2 metastases

Systematic nodal dissection

- peripheral tumors < 2 cm.: 24% LN mets
- necessary for accurate staging NSCLC
- gold standard for mediastinal staging
- confusion: radical lymphadenectomy
  lymph node sampling
- R: 4,3,2 7,8,9  L: 5,6,4 7,8,9

• 200 patients operated lung cancer
• PET-CT followed by staging mediastinoscopy and resection, if appropriate
• PET-CT correct staging 99 pts 49.5 %
  under-staged 59 29.5 %
  over-staged 42 21 %
• superior mediastinal nodes not correctly staged in 19 %

Is lobectomy standard therapy?

- LCSG: prospective randomized trial
  lobectomy versus lesser resection

- peripheral cT1N0 < 3cm
- 50% contra-indication to randomization:
  not T1 (size, pleura) not N0 (25% mediastinal LN involvement !)
- postop. morbidity and mortality equal

Ginsberg RJ. Ann Thorac Surg 1995; 60:615
Role of limited resection?

**Minimal resection = lobectomy**

Ginsberg RJ. Ann Thorac Surg 1995; 60:615
Survival pT1

Deaths / N  MST  5-Year

- pT1, <=2cm  492/ 1816  NR  77%
- pT1, >2-3 cm  582/ 1653  113  71%

Rami-Porta R. J Thorac Oncol 2007; 2:593
**T1a peripheral lung lesions**

**Treatment algorithm**

• prospective single centre trial, T1a ≤ 2 cm

• inclusion ≤ 2 cm on HRCT
  hilar, mediastinal LN ≤ 1 cm (cN0)

• 179 pts proven or suspected lung cancer - 10/97 and 09/02

• lesions: ≤ 10, 11-15, 16-20 mm

• % GGO: ≥ 50% GGO type, < 50% solid type

• procedures: wide wedge resection, segmentectomy, lobectomy

Kodama K. Eur J Cardiothorac Surg 2008; 34:1068
T1a peripheral lung lesions

Treatment algorithm

<table>
<thead>
<tr>
<th>Ø</th>
<th>type</th>
<th>procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10 mm</td>
<td>any type</td>
<td>observation → ↑ size, density</td>
</tr>
<tr>
<td>any size</td>
<td>pure GGO</td>
<td>wedge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>segmentectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(VATS) lobectomy</td>
</tr>
<tr>
<td>11-15 mm</td>
<td>GGO</td>
<td>segmentectomy + LN sampling</td>
</tr>
<tr>
<td></td>
<td>solid</td>
<td>segmentectomy + LN dissection</td>
</tr>
<tr>
<td>16-20 mm</td>
<td>GGO</td>
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<td></td>
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T1a peripheral lung lesions

Follow-up

- limited resection: no locoregional recurrences
- lobectomy: 5 (metastatic pleuritis, resection margin, LN)

<table>
<thead>
<tr>
<th>Surgery</th>
<th>DFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited resection</td>
<td>98%</td>
<td>97%</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>74%</td>
<td>80%</td>
</tr>
</tbody>
</table>

5-year limited resection 98%  
lobectomy 74%

5-year limited resection 97%  
lobectomy 80%
Mortality lung resection

- lobectomy
  - open 2 → 1% recent series
  - VATS < 1%

- pneumonectomy 4-8%
  - R > L (bronchopleural fistula)
  - ↑ induction chemoradiotherapy

Pennathur A. Curr Opin Pulm Med 2007; 13:267
Altorki K. Therapeutic modalities for small stage I lung cancers. ASCO 2008
Morbidity lung resection

- overall morbidity: 6 – 22%
  
  ↑ induction therapy
  
  up to 60% complex pneumonectomies

- complications
  
  respiratory
  
  cardiac
  
  surgical

Pennathur A. Curr Opin Pulm Med 2007; 13:267
Altorki K. Therapeutic modalities for small stage I lung cancers. ASCO 2008
Long-term results

- 5-year survival lobectomy stage I 60-70%
- local control 65-90%
- limited resection similar results peripheral T1 ≤ 2cm N0
- surgical treatment guidelines well established
- lobectomy = gold standard for comparison

Pennathur A. Curr Opin Pulm Med 2007; 13:267
Rami-Porta R. J Thorac Oncol 2007; 2:593
Against SRT in operable tumors

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- **stereotactic radiotherapy as new treatment modality**
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  - radiotherapy issues
Against SRT in operable tumors
New treatment modalities

- radiofrequency ablation (RFA)
- stereotactic radiotherapy (SRT) or stereotactic radiosurgery (SRS)
  adopted from brain irradiation but: lung is moving target!
  does not equal surgery: radiosurgery
- meta-analysis medically inoperable patients stage I NSCLC classical
  radiotherapy: 5-year survival 21%
  local recurrence: most common reason treatment failure

  Qiao X. Lung Cancer 2003; 41:1

- new fascinating strategies developed, hypofractionation
- non-randomized studies: local control ≈ surgery
- operable early stage I NSCLC? major concerns!!!
How to obtain a pathological diagnosis?

- peroperative frozen section analysis
- SRT: no precise histological diagnosis, up to 70% of patients
  
  Lagerwaard FJ. Int J Radiat Oncol Biol Phys 2008; 70:685

- ROSEL trial (Radiotherapy Or Surgery for operable Early stage non-small cell Lung cancer): no histology required; new or growing lesion with + PET sufficient

  study currently stopped

- what is irradiated? what is compared to surgery? benign lesion/cancer/ mixed or heterogeneous lesions?
Against SRT in operable tumors

74-year-old suspect lesion LUL aspergilloma!
Against SRT in operable tumors

65-year-old tumor RLL tuberculoma!
How to determine nodal staging?

- clinical staging not reliable
- clinical ≠ pathological staging; survival difference cTNM and pTNM

**Against SRT in operable tumors**


Rusch VW. J Thorac Oncol 2007; 2:603

Precise information on nodal staging will never be available!
Against SRT in operable tumors

How to evaluate response and local recurrence rate?

• radiotherapy: fibrosis, radiopneumonitis
• evaluation of response? CT-PET?
• modified RECIST criteria
  - lesion size
  - quality of lesion
  - uptake on PET

Pennathur A. J Thorac Cardovasc Surg 2009; 137:597

• no uniform agreement, no prospective validation
How to select patients for adjuvant therapy?

- pN1 or pN2 involvement: adjuvant chemo- or chemoradiotherapy
- how to select after SRT?
- no optimal treatment given
- long-term survival compromised?

Wakelee H. Semin Thorac Cardiovasc Surg 2008; 20:198
Against SRT in operable tumors

Radiotherapy issues

- no clear guidelines
- no precise selection: central lesions ↑ toxicity and ↑
  
  2-year freedom from toxicity 54% ↔ 83% peripheral

  Timmerman R. J Clin Oncol 2006; 24:4833
- 1ary endpoint? local control ↔ overall and disease-free survival
- exact dose? steep dose-response relationship
  
  local failure up to 42%

  Pennathur A. J Thorac Cardiovasc Surg 2009; 137:597

- movement of target lesion? no definite solution
Against SRT in operable tumors

Radiotherapy issues

- long-term safety SRT? radiation pneumonitis
  - rib fractures
  - chronic pain

Haasbeek CJ. Oncologist 2008; 13:309

- many concerns remain in operable patients
- compromises: diagnosis, staging, response, long-term evaluation
- thoracic surgeons co-investigators randomized trials
- currently, SRT ≠ surgery for resectable, early stage lung cancer
Against SRT in operable tumors

CONCLUSIONS

Aim = complete resection

complete irradiation? radiotherapy

• preoperative cT and cN factor unreliable
• peroperative staging: T and N factor “surgical stage”
• T1a: lobectomy vs. sublobar resection vs. SRT
• SRT operable lesions:
  many concerns remain ≠ complete resection
  compromises: diagnosis, staging, response
  long-term evaluation
Against SRT in operable tumors

- lobectomy gold standard
  - incision ↓ VATS
  - resection ↓ sublobar
  - wedge excision → segmentectomy
  + brachytherapy

- stereotactic radiotherapy (SRT) → salvage surgery
- RFA + SRT

Van Schil P. J Thorac Oncol 2010; 5:1881-2