THE PLACE OF LESS INVASIVE SURGERY IN THE TREATMENT OF LUNG CANCER

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Esmo Madrid
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• CHARACTERISTICS OF LUNG CANCER IN THE SCREENING ERA
• EVOLUTION OF SURGICAL APPROACH
• LIMITED RESECTIONS FOR NSCLC
• THE ROLE OF SABR IN FIT PTS
• CONCLUSIONS
LDCT SCREENING: DIAGNOSTIC REVOLUTION FOR LUNG CANCER

- Imaging advancement and early detection programs > more than 80% stage I and II, mean size of screen tumors 15 mm.
- Traditional surgery seems an overtreatment
- Less invasive treatment required

Stage of screening detected lung cancers COSMOS STUDY

- 95; 75%
- 17; 13%
- 7; 5%
- 9; 7%
The table presents the results from the COSMOS screening study (2005-2010, 5203 high-risk individuals) on LC (N0M0) cancer detection. The study followed 23,116 person-years of observation. The table compares the numbers of participants recalled for CT or PET in each screening round, the first primary localized cancer, and the mean size of non-solid nodules. The table highlights the following key points:

- **Baseline Round**: 5203 participants, 525 recalled for CT or PET, 160 recalled for PET, 55 first primary cancer, 43 localized cancer (N0M0), mean size 20.6 (13.6) mm, and 48 (87.3%) PET-positive non-solid nodules.
- **2nd Round**: 4822 participants, 189 recalled for CT or PET, 68 recalled for PET, 38 first primary cancer, 26 localized cancer (N0M0), mean size 13.6 (7.2) mm, and 26 (68.4%) PET-positive non-solid nodules.
- **3rd Round**: 4583 participants, 232 recalled for CT or PET, 74 recalled for PET, 39 first primary cancer, 34 localized cancer (N0M0), mean size 12.4 (7.5) mm, and 11 (28.2%) PET-positive non-solid nodules.
- **4th Round**: 4385 participants, 289 recalled for CT or PET, 62 recalled for PET, 31 first primary cancer, 23 localized cancer (N0M0), mean size 18.6 (18.6) mm, and 21 (67.7%) PET-positive non-solid nodules.
- **5th Round**: 4123 participants, 241 recalled for CT or PET, 66 recalled for PET, 12 first primary cancer, 10 localized cancer (N0M0), mean size 11.0 (4.5) mm, and 5 (41.7%) PET-positive non-solid nodules.
- **Whole Period**: 23,116 person-years of observation, 1476 recalled for CT or PET, 430 recalled for PET, 175 first primary cancer, 136 localized cancer (N0M0), mean size 16.2 (12.5) mm, and 111 (63.4%) PET-positive non-solid nodules.

Veronesi G et al: JTO 2014
DISTRIBUTION OF LUNG CANCERS ACCORDING TO VOLUME DOUBLING TIME (VDT)

Seventy five percent of cancers had a volume doubling time <400 days. 25% were slow-growing (VDT ≥400 days). 10% of them had VDT>600 days (indolent=overdiagnosis)
LUNG CANCER-SPECIFIC MORTALITY ACCORDING TO CLASSIFICATIONS OF VOLUME DOUBLING TIME (VDT)

Prevalent: cancer diagnosed at baseline CT. New (de novo): cancer diagnosed at follow-up CT. Fast-growing: cancer arising from previously identified nodule, VDT <400 days. Slow-growing: cancer arising from previously identified nodule VDT ≥400 days.
MICRO RNAs

- Short non-coding fragments of RNAs
- Function as modulators of gene expression and involved in the regulation of cellular differentiation, proliferation and apoptosis
- Expression often deregulated in human cancers in a tissue- and cancer-specific manner
- Present in human plasma in a remarkably stable form (they are protected from endogenous RNAse activity)

A signature of 13 microRNAs is able to detect LC with high sensitivity and specificity with important clinical implication for non invasive molecular diagnosis and prognostic profile
We analysed a consecutive series of clinical N0 screening detected lung malignancy to identify predictive criteria of nodal involvement.

<table>
<thead>
<tr>
<th>Preoperative PET scan</th>
<th>c-Stage T1-2N0M0 lung cancer</th>
<th>&lt; 3 cm Ø</th>
<th>Anatomical resection + lymphadenectomy</th>
<th>no prior treatment</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>SCREENING</th>
<th>CLINIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0 (91)</td>
<td>pN+</td>
</tr>
<tr>
<td>≤10mm / SUV &lt; 2</td>
<td>25</td>
</tr>
<tr>
<td>≤10mm / SUV ≥ 2</td>
<td>23</td>
</tr>
<tr>
<td>&gt;10mm / SUV &lt; 2</td>
<td>14</td>
</tr>
<tr>
<td>&gt;10mm / SUV ≥ 2</td>
<td>29</td>
</tr>
</tbody>
</table>

In cases of tumors larger than 1 cm and PET positive 17 to 22% had hilar or mediastinal lymph node unexpected metastases
But for tumor lower than 1 cm or pet negative 1/105 pts (<1%)
SECOND PRIMARIES in SCREENING

10% of patients with a screen detected tumor had multifocal disease at diagnosis.

6% has developed a new primary tumor of the lung during 5 years. These subjects, already having lung surgery, can badly tolerate a second surgery.

Veronesi G et al: JTO 2014
EVOLUTION OF SURGICAL APPROACH

Posterolateral Thoracotomy

Lateral Muscle Sparing Thoracotomy

VATS Approach

Robotic Approach
Compared to thoracothomy, VATS lobectomy was associated with improved survival (at 4 years after resection), all statistically significant. Compared with lobectomy performed by thoracotomy, VATS lobectomy for patients with early-stage NSCLC is appears to favor lower morbidity and improved survival rates.

Advantages of MIS versus open:
- Reduced pain, complications, blood transfusions and postoperative stay
- Improved quality of life, aesthetic and functional results

Compared to thoracothomy, VATS lobectomy was associated with improved 4-year survival.
<table>
<thead>
<tr>
<th>COPENAGHEN ANTERIOR APPROACH</th>
<th>POSTERIOR APPROACH</th>
<th>SINGLE PORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiene Hansen</td>
<td>William Walker</td>
<td>Diego Gonzales</td>
</tr>
</tbody>
</table>

- **POSTERIOR APPROACH**
  - Easy access to posterior hilum and lymph nodes
  - The surgeons stand posterior to the patient
  - Utility incision is made at the 6th or 7th intercostal space more posterior and camera port through the auscultatory triangle
  - Disadvantages: complex and technically demanding procedure

- **SINGLE PORT**
  - Single incision at the V is anteriorly.
  - Better view at the hilum.
  - Reduced pain
  - Both surgeons on abdominal site

- **COPENAGHEN ANTERIOR APPROACH**
  - Camera same position during procedure
  - N° 3 incisions
  - Easier to convert in emergency
  - Working channels on both side
  - Both surgeons on abdominal site
Lack of 3D vision

Diversion of true and virtual operating field

Instable surg field (camera assistant)

Bad ergonomics

Tremors amplification

Fulcrum effect

Counteractive movements
ROBOTIC SYSTEM

To overcome VATS limitations, micromechanics and robotic technology was introduced. Natural movements of the surgeon’s hands are translated into precise instrument movements inside the patient with tremor filtration. Three dimensional view offers a visual magnification that compensate the absence of haptic feedback.

Robotic system can make MIS more accessible to surgeons in training and can expand indications.
4 arms, 4 incisions
NO CO2 Insufflation
Utility incision at the beginning
Anterior approach

3 arms, 4 incision
CO2 insufflation
Utility incision at the end
Posterior approach

4 arms, 5 incisions
CO2 Insufflation
Utility incision at the end
Posterior approach
# ROBOTIC LOBECTOMIES: CASE SERIES

<table>
<thead>
<tr>
<th>Lead Author</th>
<th>Year</th>
<th>No. Pts</th>
<th>MOT</th>
<th>LOS (min)</th>
<th>Compl. (Days)</th>
<th>Mortality (%)</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park</td>
<td>2006</td>
<td>30</td>
<td>218</td>
<td>4.5</td>
<td>26</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Melfi</td>
<td>2004</td>
<td>107</td>
<td>220</td>
<td>5</td>
<td>na</td>
<td>1</td>
<td>na</td>
</tr>
<tr>
<td>Gharagozloo</td>
<td>2009</td>
<td>100</td>
<td>216</td>
<td>4</td>
<td>21</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Veronesi</td>
<td>2010</td>
<td>54</td>
<td>224</td>
<td>4.5</td>
<td>20</td>
<td>0</td>
<td>9.4</td>
</tr>
<tr>
<td>Park, Melfi, Veronesi</td>
<td>2011</td>
<td>325</td>
<td>210</td>
<td>5</td>
<td>25</td>
<td>na</td>
<td>8</td>
</tr>
<tr>
<td>Veronesi</td>
<td>2012</td>
<td>91</td>
<td>213</td>
<td>5</td>
<td>20</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td><strong>CPRL / CPRS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dylewski</td>
<td>2011</td>
<td>165 / 35</td>
<td>90</td>
<td>3</td>
<td>26</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>Cerfolio</td>
<td>2011</td>
<td>106 / 16</td>
<td>132</td>
<td>2</td>
<td>27</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

CPRL – Complete port robotic lobectomy  
CPRS – Complete port robotic segmentectomy  
RAL – Robotic assisted lobectomy
ROBOTIC LOBECTOMY FOR NON-SMALL CELL LUNG CANCER (NSCLC): LONG-TERM ONCOLOGIC RESULTS
B.J. Park, F. Melfi, P. Maisonneuve, L. Spaggiari, R Da Silva, G. Veronesi
Journal of Thoracic and Cardiovascular Surgery 2011

Pathologic stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>325</td>
<td>54%</td>
</tr>
<tr>
<td>IB</td>
<td>176</td>
<td>(54%)</td>
</tr>
<tr>
<td>IIA</td>
<td>72</td>
<td>(22%)</td>
</tr>
<tr>
<td>IIB</td>
<td>41</td>
<td>(13%)</td>
</tr>
<tr>
<td>IIIA</td>
<td>15</td>
<td>(5%)</td>
</tr>
<tr>
<td>II</td>
<td>21</td>
<td>(6%)</td>
</tr>
</tbody>
</table>

Log-rank P = 0.0001
Pathologic nodal upstaging occurred in 33 patients (10.9%)

<table>
<thead>
<tr>
<th></th>
<th>Robot</th>
<th>Vats</th>
<th>Thoracotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN1</td>
<td>6.6%</td>
<td>5.2%</td>
<td>7.5%</td>
</tr>
<tr>
<td>pN2</td>
<td>4.3%</td>
<td>7.1%</td>
<td>8.8%</td>
</tr>
<tr>
<td>cT1a</td>
<td>3.5</td>
<td>5.7%</td>
<td>11.5%</td>
</tr>
<tr>
<td>cT1b</td>
<td>8.6</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>cT2a</td>
<td>10.8</td>
<td>5.7</td>
<td></td>
</tr>
</tbody>
</table>

The rate of nodal upstaging for robotic resection appears to be superior to VATS and comparable to thoracotomy.
RLL AFTER CHEMOTHERAPY FOR N2 DISEASE
Case-control evaluation: 53 Robotic and 35 VATS

Similar surgical and postoperative outcomes

Significantly shorter duration of narcotic use and earlier return to normal activities after robotic approach

The ability to perform mediastinal lymph node dissection was similar in the VATS and robotic approaches, however, robotics gave greater confidence in dissecting N1 lymph nodes adjacent to the pulmonary artery, allowing easier and safer passage of the stapler...
Learning curve robot and vats surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Robotic surgery</th>
<th>VATS</th>
<th>VATS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First 15&lt;sup&gt;th&lt;/sup&gt;</td>
<td>16&lt;sup&gt;th&lt;/sup&gt;-75&lt;sup&gt;th&lt;/sup&gt;</td>
<td>76&lt;sup&gt;th&lt;/sup&gt; onward</td>
</tr>
<tr>
<td>Number of operations</td>
<td>15 (20.0)</td>
<td>60 (10.0)</td>
<td>96 (3.1)</td>
</tr>
<tr>
<td>Number of conversions (%)</td>
<td>3 (20.0)</td>
<td>6 (10.0)</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td>Number of complications (%)</td>
<td>5 (33.3)</td>
<td>14 (23.3)</td>
<td>24 (25.0)</td>
</tr>
<tr>
<td>Major/minor</td>
<td>4/1</td>
<td>9/5</td>
<td>15/7</td>
</tr>
<tr>
<td>Median operating time, minutes (range)</td>
<td>259 (145-370)</td>
<td>214 (116-304)</td>
<td>177 (69-306)</td>
</tr>
<tr>
<td>Median postoperative stay, days (range)</td>
<td>6 (5-24)</td>
<td>4 (3-23)</td>
<td>5 (2-14)</td>
</tr>
<tr>
<td>Median number of lymph nodes removed at first level (range)</td>
<td>6 (2-13)</td>
<td>8 (0-23)</td>
<td>7 (0-27)</td>
</tr>
<tr>
<td>Median number of lymph nodes removed at second level (range)</td>
<td>3 (0-18)</td>
<td>5 (1-25)</td>
<td>6 (2-21)</td>
</tr>
<tr>
<td>Patients with no lymph node removed at second level (%)</td>
<td>1 (6.7)</td>
<td>0 (0.0)</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td>Number of upstage CN0&gt;pN1</td>
<td>2/11 (18.2)</td>
<td>2/59 (3.4)</td>
<td>4/84 (4.8)</td>
</tr>
<tr>
<td>Number of upstage CN0&gt;PN2</td>
<td>1/11 (9.1)</td>
<td>2/59 (3.4)</td>
<td>6/84 (7.1)</td>
</tr>
</tbody>
</table>
Higher costs of Robotics versus Vats will be justified if robotics will allow an higher transition from thoracotomy to minimally invasive surgery for early and locally advanced stage lung cancer.
SUBLOBAR RESECTION and SABR FOR EARLY STAGE
Radical sublobar resection for small-sized non–small cell lung cancer: A multicenter study

Morihito Okada, MD, PhD,a Teruaki Koike, MD, PhD,b Masahiko Higashiyama, MD, PhD,c Yasushi Yamato, MD, PhD,b Ken Kodama, MD, PhD,c and Noriaki Tsubota, MD, PhDa

Nonrandomized study for patients with a peripheral cT1N0M0 NSCLC < 2 cm able to tolerate a lobectomy
Sublobar resection group (n 305) compared with lobar resection group (n 262)

Conclusion:
Extended segmentectomy should be considered as an alternative for patients with cT1N0M0 NSCLC of 2 cm or smaller
Meta-analysis of intentional sublobar resections versus lobectomy for early stage non-small cell lung cancer

Christopher Cao, Sunil Gupta, David Chandrakumar, David H. Tian, Deborah Black, Tristan D. Yan

Overall survival: sublobar vs. lobectomy. HR 0.91 (0.6-1.2)

Overall survival: segmentectomy vs. lobectomy. HR 1.04 (0.7-1.4)
AIM: to evaluate the “non inferiority” in overall survival of sublobar resection compared to lobectomy in peripheral Stage IA NSCLC ≤ 2 cm
Preoperative criteria: Suspicious or proven NSCLC; Lung nodules ≤ 2 cm; N0 at preoperative PET/CT; N0 prior treatment for lung cancer

Intraoperative criteria: Diagnosis of NSCLC; Lesion suitable for a limited resection; No lymph node at FS when size > 1 cm and SUV positive; Negative margins

Stratification
Nodule Size (≤1 versus > 1 cm)
PET on nodule (positive versus negative)

Wedge or segmentectomy
Lobectomy with SND

Study design and coordinator: G. Veronesi
Thoracoscopic segmentectomy is a safe and feasible procedure for experienced TS, comparing favorably with OS by reducing hospital length of stay.
Robotic anatomic lung segmentectomy is feasible, safe and reproducible in different centres
Robotic system, by improving ergonomic, surgeon view and precise movements, may make minimally invasive segmentectomy easier to adopt and perform
• 63 years old woman, heavy smoker, enrolled in a CT screening program.

• 2011 detection of a non solid lesion of the Left Upper Lobe, centrally located, PET neg, slow growing. Final diagnosis: minimally invasive multifocal adenocarcinoma
They compared patterns of failure between lobar resection (lobectomy or pneumonectomy) and stereotactic body radiation therapy (SBRT) for patients with clinical stage I non-small-cell lung cancer (NSCLC).

Clinical stage I NSCLC: lobar resection (n = 260) SBRT (n = 78)

Lobar resection patients were younger, healthier, and had superior pulmonary function, whereas most of the patients in the SBRT group had T1 tumors. Final pathology upstaged 32.7% of surgery patients, 20.0% received adjuvant chemotherapy. No SBRT patients received adjuvant chemotherapy.

Cause-specific survival (CSS, 81.3% versus 75.3%, p = 0.923) was similar. In a T-stage matched comparison, there was no significant difference in patterns of failure or CSS, whereas OS favored surgery.

CONCLUSION:
Lobectomy/pneumonectomy or SBRT results in comparable patterns of failure for clinical stage I NSCLC. In this retrospective comparison, OS was superior for surgery, though CSS was similar. Randomized trials are necessary to control for fundamental differences in comorbidity, which impact interpretation of both tumor control and survival.
There were at least two attempts of randomised studies comparing surgery to SABR in operable patients

1) A randomized study comparing CyberKnife treatment to surgical resection for Stage I NSCLC (STARS) based in MD Anderson Cancer Center in the United States

2) A randomized Phase III trial, Radiosurgery or Surgery for operable Early-stage (Stage IA) non-small-cell Lung cancer (ROSEL) based in VU University Medical Center in Netherlands (Hurkmans et al Radiation Oncology 2009)
PHASE III RANDOMIZED TRIAL OF SURGICAL RESECTION VERSUS STEREOTACTIC ABLATIVE RADIOTHERAPY (SABRT) FOR EARLY STAGE LUNG CANCER LESS THAN 2 CM IN SIZE AND SUV LESS THAN 2.5.

**Preoperative evaluation:**

1) Suspicious or proven NSCLC
2) Lung nodules peripheral ≤ 2 cm
3) Negative nodes at preoperative PET/CT
4) N0 prior treatment for lung cancer
5) Low uptake at CT/PET (less than 2.5)

**RANDOMIZATION**

Subjects will be stratified according to:
Nodule size (≤1 versus > 1 cm)
Nodule characteristics at PET (negative versus positive by visual assessment)

- SABRT
- Lobectomy or segmentectomy plus systematic nodal dissection

**Primary objectives:**
Disease free survival
LETS THINK TO WHAT ROBOTICS WILL BE AND NOT TO WHAT ROBOTICS IS!!

ROBOTIC STAPLERS
ROBOTIC SUCTION
FLUORESCENCE VISION
DUAL CONSOLE (TANDEM SURGERY – TRAINING)
SINGLE PORT
TACTILE FEEDBACK
DISTANCE TELESURGERY
DISTANCE PROCTORING ……and ….
LUNG CANCER

PREVENTION AND TOBACCO FREE CIGARETTE

SCREENING WITH LD CT

MOLECULAR DIAGNOSIS

CONSERVATIVE SURGERY

MINIMALLY INVASIVE ROBOTIC SURGERY

RADIOSURGERY
SUMMARY 1

- Lung cancer is diagnosed in early stage more frequently than in the past. Thus surgeons are faced to offer treatments that are proportionate to the disease.

- MIS for early stage has important advantages for patients compared to open surgery

- Robot-assisted approach is more comfortable for surgeons than manual vats, N1 upstaging after robotics is similar to open surgery, indication of MIS may be expanded

- High capital and running costs remain the main disadvantages of robotics
• Limited resection are under evaluation for peripheral NSCLC lower than 2 cm in randomised trials

• Radical lymph node dissection may be avoided in nsclc with negative CT/PET or size less than 1 cm.

• A randomised trial of SABR versus Surgery can be proposed for patients with very early stages