MOTION MANAGEMENT FOR LUNG and ABDOMINAL TUMORS

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Erasmus MC – Cancer Institute, Rotterdam
Introduction

1. INTRODUCTION
2. BONE METASTASES
3. ABDOMINAL TUMORS
   1. LNN
   2. PANCREAS
4. LUNG TUMORS
At Erasmus MC: 2 M6's Mantis Polaris (+ in CT room CT)
The CyberKnife® System at EMC

Clinical indications

**Intracranial**
Brain, primary tumors,
trigeminal neuralgia,
arteriovenous malformations

**H&N**

**Spine**
Spinal metastasis,
benign tumors, spinal AVMs

**Breast**

**Lung**
Early stage and advanced
primary lung cancer,
pulmonary metastases

**Pancreas**
Inoperable patients,

**Liver**
Liver metastases,
inoperable primary liver cancer

**Pelvic Bone & Ribs**

**Lymphnodes**

**Prostate**
Low and intermediate risk
prostate cancer, monotherapy

**Long Bone**
Treatment Modalities

Targets that not move

1. (Skull tracking)
2. X-sight spine
3. Fiducial tracking (eg: the 1st rib)

Moving targets: Synchrony

1. X-sight lung
2. Fiducial tracking

Movement over time

1. (In Tempo (prostate))
Image guidance during treatment delivery

**IGRT & Cone Beam CT**
Correction limited to only pre-treatment alignment

Hoogeman, Mischa, ErasmusMC, Daniel den Hoed cancer Center, Rotterdam, The Netherlands
Image guidance during treatment delivery

**IGRT & Cone Beam CT**
Correction limited to only pre-treatment alignment

**Intrafraction Verification**
Large doses delivered between corrections

Hoogeman, Mischa, ErasmusMC, Daniel den Hoed cancer Center, Rotterdam, The Netherlands
Image guidance during treatment delivery

IGRT & Cone Beam CT
Correction limited to only pre-treatment alignment

Intrafraction Verification
Large doses delivered between corrections

Image Capture
Target Shift Correction
Beam Delivery

Immobilized Spine Intra-Fraction Target Motion

CyberKnife® System Image Guidance
Minimal dose delivered between corrections

Hoogeman, Mischa, ErasmusMC, Daniel den Hoed cancer Center, Rotterdam, The Netherlands
Oligometastasis

clinically treated patient: 2*12 Gy
Oligometastases: examples (2)
Oligometastases: examples (3)

• 2*12 Gy
Oligometastasis

- Oligometastases:
- clinically treated patient (5 x 9 Gy)
Promising Local Control Rates and activity on symptoms control

Lack of information about patterns of failure

Not negligible G3-G4 toxicity (3-14%) raise concern about the benefit of this strategy

Even though most patients treated locally using SBRT for lymph nodes metastases eventually fail at other sites, the local control provided by this initial experience may be potentially significant for preserving quality of life and delaying further systemic treatments
SBRT for abdominopelvic oligometastases

Clinical & Experimental Metastasis
https://doi.org/10.1007/s10585-018-9922-x

RESEARCH PAPER

Locoregional control and survival after lymph node SBRT in oligometastatic disease

Mauro Loi¹ • Michael Frelighuysen¹ • Natalie Desiree Klass¹ • Esther Oomen-De Hoop¹ • Patrick Vincent Granton¹ • Joachim Aerts² • Cornelis Verhoef³ • Joost Nuyttens¹

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ORIGINAL ARTICLES: RADIOTHERAPY

Acute toxicity of the bowel after stereotactic robotic radiotherapy for abdominopelvic oligometastases

Michael Frelighuysen, Wilco Schillemans, Lieke Hol, Cornelis Verhoef, Mischa Hoogeman & Joost Jan Nuyttens

Pages 480-484 | Received 18 Jul 2017, Accepted 06 Sep 2017, Published online: 18 Sep 2017
SBRT for Lnn

91 patients
no prostate ca
1/3 colorectal ca

Most treated
6*8 Gy
5*9 Gy

4-years Su: 43%

Loi et al, 2018
SBRT for Lnn

- Local control and locoregional control: 79%
SBRT for Lnn

- Local Failure Probability (%) vs Tumor diameter (mm)
- Log odds LR
- 95%CI
- Local Control
- Local Relapse
84 patients with solitary or oligometastatic tumors

- **Location:**
  - Para-aortic or iliac lymph nodes: 65 patients
  - Metastases in the abdomen or pelvis: 19 patients
Results: toxicity

- No acute or late grade 4 or 5 toxicity

- Acute toxicity:
  - Nausea: 20 patients (24%)
    - Grade 3: 3 patients (4%)
    - Grade 2: 7 patients (8%)
    - Grade 1: 10 patients (12%)
    - (1 patient was admitted due to nausea & vomiting)
  
  - Acute diarrhea: 11 patients (13%)
    - Grade 2: 4 patients (5%)
    - Grade 1: 7 patients (8%)
Results: acute bowel toxicity

- Recalculated EQD2
- V50: volume receiving 50 Gy EQD2
LAPC1 trial (Erasmus MC)

Study Design

- First chemotherapy Folfirinox: 8 cycles = 4 months
- Then re-evaluation with CT scan=> no metastases
- SBRT: 5*8 Gy prescribed to the 80%
- Accrual (53) is reached
Pancreas
**Delineation**
- **CE-CT 1.5 mm**
- **SBRT margins**
  - GTV->CTV: 5 mm
  - CTV-> PTV: 2 mm

**Organ at Risk** | **Dmax**
--- | ---
Spinal Cord | 5.5 Gy per fraction= 27.5 Gy
Liver | 700 cc must receive < 17.5 Gy.
Bowel | 7 Gy per fraction = 35 Gy
Kidney | 1/3 of both kidneys may not exceed 15 Gray in 5 fractions
Stomach | 7 Gy per fraction = 35 Gy
Stomach

Duodenum
Results LAPC-1 trial

- We included 53 patients
- 39 patients were treated with SBRT
- OS of the whole group was 18 months

- 7 resection (14%) ->
  - all were complete resections
- 3 CR (6%)
- 2 almost complete response (4%)
- 2 PR (4%)
- 1 grade 5 toxicity
Overall Survival patients treated with SBRT
IT WORKS NICELY ON METASTASIS, TOO!
Tumor motion
Target volume: moving target

Normal breathing
Target definition

ITV based target volume

Real-time tumor tracking

- GTV
- CTV
- ITV
- PTV
The Synchrony System

CYBERKNIFE®
SYNCHRONY™
Respiratory Tracking System

ACCURay®
Synchrony and the patient
LOT

• Xsight lung
  • 2 view -> not feasible -> fiducial placement
    • GTV-> PTV: 5 mm
  • 1 view
    • ITV -> PTV: 5 mm
  • 0 view
    • ITV (4 fase: 0in, 50in, 100in, 50ex)
Xsight lung
Fiducial placement for lung tumors

• In total, 323 markers were placed in or around 99 tumors.
• We used 5 methods to place fiducials:
  1. Percutaneous intrapulmonary method:
     59 fiducials for 21 tumors (median 3 fiducials/tumor)
  2. Percutaneous extrapulmonary method:
     14 fiducials for 3 tumors (median 5 fiducials/tumor)
  3. Intravascular coil method:
     239 coils for 71 tumors (median 3 fiducials/tumor)
  4. Bronchoscopic method:
     4 fiducials in 1 tumor
  5. Endoscopic ultrasound method (EUS):
     9 fiducials in 3 tumors
Fiducial Implantation: EMC

• Intravascular Coil placement:
Fiducials: complications and Xsight lung

Side effects of fiducial placement

- 6 patients had a pneumothorax (6 %)
  3 patients needed a thoraxdrain (3 %)

- Overall RTOG grade 3 toxicity: 3 patients (3 %)
Own data

- Results from the first 206 patients
- With peripheral early stage lung cancer tumors.
  - Smaller than 3 cm (T1): 108 tumors
  - Greater than 3 cm (T2): 52 tumors
  - Greater than 7 cm (T3): 3 tumors
  - Range: 10-100 mm
- Pathology in 42% of the patients

Mohkles, 2014, ann surg onc
Patient demographics

- Median age: 74 years,
  
  26% ≥ 80 years old!

- Charlson Comorbidity Score:
  - Group 1 (0-2): 54%
  - Group 2 (3-4): 33%
  - Group 3 (>4): 13%

- Cumulative Illness Score:
  - Group 1 (0-4): 44%
  - Group 2 (5-6): 20%
  - Group 3 (>6): 36%
Radiotherapy treatment: dose

- GTV + 5mm = PTV
- Total Dose:
  - First used schedules:
    - 36 Gy (3*12 Gy; 66 Gy\textsubscript{10}): 1 tumor
    - 45 Gy (3*15 Gy; 94 Gy\textsubscript{10}): 12 tumors
    - 50 Gy (5*10 Gy; 83 Gy\textsubscript{10}): 1 tumor
  - Later used schedules:
    - 60 Gy (3*20 Gy; 150 Gy\textsubscript{10}): 186 tumors
    - 60 Gy (5*12 Gy): 5 tumors
- The dose to the PTV was usual prescribed to the 80% isodose line (range: 70-90%).
Target volume: real time tumor tracking
Follow up & Results: Local control

- 2-years local control:
  - 3*20 Gy: 91%
  - 3*15 Gy: 76%
  - $P = 0.18$
Follow up & Results: Overall Survival

- 206 patients
- 2 years Overall Survival: 68%
- 4 years Overall Survival: 41%
Lung metastasis

Patients: 206 with 326 tumors

<table>
<thead>
<tr>
<th>Age, median (range)</th>
<th>68 year (28 – 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (m/v)</td>
<td>120 / 86</td>
</tr>
<tr>
<td>Charlson comorbidity index, median (range)</td>
<td>1 (0 – 13)</td>
</tr>
</tbody>
</table>

Presentation meta’s

<table>
<thead>
<tr>
<th>Synchronous</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metachronous</td>
<td>146</td>
</tr>
</tbody>
</table>

Distribution meta’s

<table>
<thead>
<tr>
<th>Only in the lung</th>
<th>119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrapulmonaryal + lung</td>
<td>87</td>
</tr>
</tbody>
</table>

DFS

<table>
<thead>
<tr>
<th>≤ 3 jaar</th>
<th>153</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 3 jaar</td>
<td>53</td>
</tr>
</tbody>
</table>

Follow-up, median (range)

| 23 mnd (1 – 100) |

A. Sharma 2018, Acta Oncologica
# Lung metastasis

## Patiënts

<table>
<thead>
<tr>
<th>Primaire tumor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>117</td>
</tr>
<tr>
<td>Lung</td>
<td>36</td>
</tr>
<tr>
<td>Melanoma</td>
<td>11</td>
</tr>
<tr>
<td>other</td>
<td>41</td>
</tr>
</tbody>
</table>

**Total metastasis in the body**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
</tr>
<tr>
<td>≥ 2</td>
<td>153</td>
</tr>
</tbody>
</table>

**Pre SBRT chemo**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>100</td>
</tr>
<tr>
<td>No</td>
<td>106</td>
</tr>
</tbody>
</table>
Results: survival

- 2 year: 63%
- 3 year: 47%
- 5 year: 30%

Median OS: 32 mnd
Results: survival

![Survival Curve]

- Cum Survival
- Time (months)
- p=0.023
Definition of Central tumors

- 2 cm from …
Examples of central tumors
CENTRAL LUNG TUMORS

• Accuracy is very important
• Organs at risk
  • Oesophagus
  • Main bronchus

• The Cyberknife is the best Linac to use for these tumors
  • Xsight lung
  • Fiducial tracking
  • Spine tracking

• BE SURE YOU DO NOT MISS THE TARGET!
Central tumors: Patients and dose

- Tumor close to main stem bronchus (dose escalation):
  - 45 Gy (5*9 Gy; 71 Gy_{10}): 6 tumors
  - 50 Gy (5*10 Gy; 83 Gy_{10}): 15 tumors
  - 60 Gy (5*12 Gy; 110 Gy_{10}): 22 tumors

  -> Nowadays we use 5*11 Gy (due to MC-algorithm)

- Tumor close to oesophagus (often mediastinal):
  - 48 Gy (6*8 Gy; 72 Gy_{10}): 15 tumors
  - Maximum dose to the main stem bronchus or trachea: 8 Gy/fr
  - Maximum dose to oesophagus: 6 Gy/fr

  -> Nowadays we use 7*7 Gy (with MC-algorithm)

- The dose to the PTV was prescribed to the 70-90% isodose line (Median 80%).

Nuyttens et al. Radiother Oncol. 2012
Follow up & Results: Survival

3-years overall survival:
- Oligometastasis: 54%
- Early Stage Lung Cancer: 48%
- Local control at 2 years with total dose more than 50 Gy: 85%

- 56 patients
- 58 tumors

Nuyttens et al. Radiother Oncol. 2012
Central Tumors: Dose to organs and toxicity

<table>
<thead>
<tr>
<th>Organ</th>
<th>Median Dmax in EQD2 (range)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main bronchi</td>
<td>148 (78–236)</td>
<td>43</td>
</tr>
<tr>
<td>Trachea</td>
<td>101 (83–131)</td>
<td>9</td>
</tr>
<tr>
<td>Esophagus</td>
<td>88 (68–112)</td>
<td>18</td>
</tr>
<tr>
<td>Plexus brachialis</td>
<td>83 (73–90)</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 3
Acute and late complications (number of patients).

<table>
<thead>
<tr>
<th></th>
<th>Acute complications</th>
<th>Late complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Thoracic pain</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>11</td>
<td>6</td>
</tr>
</tbody>
</table>

No severe acute or late toxicity
Central tumors: Patients and dose

- We made an update
  - 128 patients
  - 137 central tumors
    - 79 tumors -> primary non-small-cell-lung-cancer
    - 58 tumors -> metastasis
  - All patients were recalculated with Monte Carlo

Duijm, Sem in Rad Onc, 2016
Dose and Volume of the Irradiated Main Bronchi and Related Side Effects in the Treatment of Central Lung Tumors With Stereotactic Radiotherapy

Marloes Duijm, W. Schillemans, Joachim G. Aerts, MD, PhD, B. Heijmen, and Joost Jan Nuyttens

128 patients

• 137 central tumors
  • 79 tumors -> primary non-small-cell-lung-cancer
  • 58 tumors -> metastasis

• All patients were recalculated with Monte Carlo
Follow up & Results: Survival: update

5-years overall survival around 20%
Broncheal tree toxicity

Toxicity all grade 1:
- Stenosis
- Occlusion
- Occlusion + atelectasis

Seminars in Rad Onc, 2016
### Broncheal tree toxicity

**Table 4 Volumes and Dose of Irradiated Bronchi Related to Side Effects**

<table>
<thead>
<tr>
<th></th>
<th>$D_{\text{max}}$</th>
<th>$\text{EQD}_2$</th>
<th>$D_{\text{max}}$</th>
<th>BED</th>
<th>$V_{65}$</th>
<th>$\text{EQD}_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trachea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean with side effects</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean without side effects</td>
<td>93</td>
<td>155</td>
<td>1.063</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of structures with side effects</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Main bronchus or bronchus intermedius</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean without side effects</td>
<td>105</td>
<td>175</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean with side effects</td>
<td>116</td>
<td>194</td>
<td>2.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of structures with side effects</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td>0.1</td>
<td>0.1</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Upper-, middle-, and lower bronchi</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean without side effects</td>
<td>113</td>
<td>189</td>
<td>0.7</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean with side effects</td>
<td>143</td>
<td>239</td>
<td>1.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of structures with side effects</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td></td>
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</tr>
<tr>
<td>$P$ value</td>
<td>&gt;0.00001</td>
<td>&gt;0.00001</td>
<td>0.007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Segmental bronchi</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean without side effects</td>
<td>121</td>
<td>202</td>
<td>0.326</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean with side effects</td>
<td>135</td>
<td>225</td>
<td>0.438</td>
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<tr>
<td>Percentage of structures with side effects</td>
<td>37</td>
<td>37</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td>0.011</td>
<td>0.011</td>
<td>0.008</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Oesophagus toxicity

Nuyttens, Sem Rad Onc, 2016
Conclusion

• Easy to treat bone and spine metastases
• LNN
  • Excellent Survival
  • Low toxicity
• Pancreatic tumors
  • Select your patients
  • Good outcome
  • Low toxicity
General Lung Conclusions

Stereotactic Radiotherapy is better than Conventional RT:

Outcome for **peripheral tumors:**
- With SBRT: excellent local control: > 90% at 2 years

Outcome of **Central Tumors:**
- Excellent survival, especially for oligometastatic tumors

Outcome of **Lung metastases:**
- Excellent survival!
Thanks to

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M. Hoogeman
H. Marijnissen
E. De Klerck
L. Luthart
D. De La Bije
C. De Pan
H. Joosten

Erasmus bridge, Rotterdam