Endobronchial Intra- Luminal Brachytherapy (ILT)

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DISCLOSURE OF INTEREST

• I have no actual or potential conflict of interest in relation to this program/presentation’
Overview

• Background & evidence
• Technique
• Case Studies
• Twin-line applications
• Summary
What is brachytherapy

- Radioactive source placed within or close proximity to tumour
- Geometric advantage, relative sparing of normal tissues
- Non-uniform radiation field
- Lower dose rate further away → differential cell killing
- Precise source placement to irradiate small volumes
Types of brachytherapy

- Interstitial, eg prostate
- Intracavity, eg cervix, bronchus
- Surface applications (moulds), eg skin
History of ILT

- 1921 Yankhauer inserted radium capsules (radon-222) via rigid scope

- 1964 Henschke developed remote after-loading with iridium-192. need for GA
History of ILT

• 1980s remote afterloading via plastic catheter tube inserted by flexible bronchoscopy

• Iridum-192 HDR by microselectron
Endobronchial therapies

- Surgical:
  - Neodymium-YAG laser debulking
  - Tracheo-bronchial stents
  - Cryotherapy
- Medical:
  - Photodynamic therapy
  - ILT (+/- EXBRT)
Indications: Radical

- Radical (3 successive weekly fractions):
  - Superficial T1N0M0 NSCLC
  - CIS biopsy proven and limited in extent
  - Localised tumour rec at surgical RM

- NSCLC prior to radical EXBRT to re-expand lung (single fraction)
Indications : Palliative

- Palliative (single fraction): (+/- EBXRT)
  - Symptomatic endoluminal disease NSCLC
  - Endobronchial metastasis from distant primary
  - Direct invasion from malignant node
  - Post debulk +/- stent insertion

- SOB due to collapse
- Haemoptysis
- Intractable cough
## Dose & Fractionation

<table>
<thead>
<tr>
<th>Disease site</th>
<th>Technique</th>
<th>External Beam Dose</th>
<th>Brachytherapy prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Radical</td>
<td>HDR MicroSelectron ILT (prescribed to 10mm)</td>
<td>No previous XRT</td>
<td>800-1000cGy weekly x 3</td>
</tr>
<tr>
<td>Lung Radical</td>
<td>HDR MicroSelectron ILT (prescribed to 10mm)</td>
<td>No previous XRT</td>
<td>Re-inflation before radical XRT 500 – 1000cGy x 1</td>
</tr>
<tr>
<td>Lung Palliative</td>
<td>HDR MicroSelectron ILT (prescribed to 10mm)</td>
<td>No previous palliative XRT</td>
<td>1000 – 1500cGy x 1</td>
</tr>
<tr>
<td>Lung Palliative</td>
<td>HDR MicroSelectron ILT (prescribed to 10mm)</td>
<td>Previous palliative XRT</td>
<td>1000 – 1500cGy x 1</td>
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<tr>
<td>Lung Palliative</td>
<td>HDR MicroSelectron ILT (prescribed to 10mm)</td>
<td>Previous radical XRT</td>
<td>500 – 750cGy x 1</td>
</tr>
</tbody>
</table>
Effective in Palliation

- Christie series, n=50
- Haemoptysis relieved in 24/28 pts (86%)
- SOB relieved in 21/33 pts (64%)
- Cough relieved in 9/18 pts (50%)
- Radiological collapse resolved in 11/24 pts

Intraluminal irradiation for the palliation of lung cancer with the high dose rate micro-Selectron. Burt PA; O'Driscoll BR; Notley HM; Barber PV; Stout R. Thorax 1990 Oct;45(10):765-8.
Effective as Radical

- n= 106 patients not eligible for surgery or EXBRT
  - 43 relapse after surgery, 27 relapse after EXBRT, 36 early lung cancer poor lung FTs
- 6 x weekly 5 or 7 Gy
- CR rate at 3 mths was 59%
- 3YS and 5YS 47.4 and 24%
- 5 toxic deaths (2 MFH, 3 bronchial necrosis).
- long-term cause-specific survival 50% - ‘could be considered curative’.

Effective as Radical

- 24-35Gy in 4-6 fractions
- 94% complete endoscopic resp at 3mths
- 2YS 57%, 5YS 29% (81%, 56% cancer specific)
- 5% MFH, 20% late bronchitis, 3.5% necrosis

Christie Radical case series

- 1997-2007, n=37
  - M:F 32:3
  - Ages 46 – 81 (mean 67, median 66)

<table>
<thead>
<tr>
<th>Histology</th>
<th>no</th>
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<tr>
<td>Squamous cell ca</td>
<td>19</td>
</tr>
<tr>
<td>CiS</td>
<td>8</td>
</tr>
<tr>
<td>NSCLC</td>
<td>2</td>
</tr>
<tr>
<td>Adenoca</td>
<td>1</td>
</tr>
<tr>
<td>Adenoid Cystic</td>
<td>1</td>
</tr>
<tr>
<td>Clear cell</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
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</table>

- MS 15.5 months, 2YS 38.5%
- MFH rate 8%
Palliate by ILT or EXBRT?

- Christie RCT 1989-93, n=99 randomised
- 1° endpt symptom relief, acute & late SE, QoL scores
- Better Sx relief with XRT but more acute morbidity
- Better duration relief with XRT (28% had ILT median 304 days later) than ILT (51% had XRT median 125 days later)
- MS 287 vs 250 days
XRT preferred to ILT as initial treatment in better PS pts → better palliation and OS

Stout, Barber, Burt et al, R+O 2000 (56), 323-327
Laser alone?

- Laser + ILT vs laser alone

ILT Cochrane Meta-analysis

- 13 RCTs
- EXBRT alone is more effective for palliation than ILT alone.
- No conclusive results that ILT plus EXBRT improved symptom relief over EXBRT alone. No conclusive evidence to recommend ILT with EXBRT, chemotherapy or Nd-YAG laser.
- For patients previously treated by EXBRT who are symptomatic from recurrent endobronchial central obstruction, ILT may be considered.

Cautions

- Medically unfit for bronchoscopy
- Bulky disease needing surgical airway management
- Extrinsic compression
- Proximity to major vessel
- Invasion into adjacent organ → risk fistulation
- Heavily pre-irradiated or laser debulked
Complications

- Epistaxis, haemorrhage
- Chest infection
- Hypoxia
- Cardiac
- Pneumothorax
- Bleeding
- Treatment related
  - Radiation bronchitis possibly → stenosis
  - Fistulation
  - MFH
Christie morbidity data

- 1988-92, n=406
- 32 pts died of MFH. Risk factors were 20Gy as opposed to 15Gy, 2nd ILT in same area first, prior laser treatment
- MFH peaked 9-12 mths after ILT

Technique: Localisation

- Bronchoscopy
- Epidural catheter
- Adrenaline
- 2mm diameter applicator via biopsy channel
- Applicator secured to nose
- Guidewire changed to a RMW
Technique – RT planning

- AP & Lat CXR to verify catheter position

- Oncologist localises treatment volume on CXR using 1cm scale on RMW

- Length and prescription dose determine dwell time at 5mm increments

- Treatment prescribed and microselectron machine programed
Treatment “Planning”

- Oncologist localises treatment volume on CXR based on bronchoscopy findings
- 1cm scale on Radiographic marker wire (RMW)
- Length and prescription dose determine
- Treatment parameters calculated by hand by 3 independent people
Standard line source plan

- Dwell time is the same for each source position
- 5mm stepsize between dwells
- Cigar shaped 100% dose distribution
- 10.5 cm$^3$ treated - Small area - Large dose
## Dwell times from BT.4.22

### Table 1. Dwell times for Source Serial Number D36E4576

(Reference Strength: 10.58 $\mu$Gy.s$^{-1}$ on 9th November 2012 at 15:00)

<table>
<thead>
<tr>
<th>Lengths (cm)</th>
<th>750cGy</th>
<th>800cGy</th>
<th>1000cGy</th>
<th>1500cGy</th>
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<tbody>
<tr>
<td>4</td>
<td>14.6</td>
<td>15.6</td>
<td>19.5</td>
<td>29.2</td>
</tr>
<tr>
<td>5</td>
<td>13.7</td>
<td>14.6</td>
<td>18.3</td>
<td>27.4</td>
</tr>
<tr>
<td>6</td>
<td>13.1</td>
<td>14.0</td>
<td>17.5</td>
<td>26.3</td>
</tr>
<tr>
<td>7</td>
<td>12.8</td>
<td>13.6</td>
<td>17.0</td>
<td>25.5</td>
</tr>
<tr>
<td>8 or 9</td>
<td>12.4</td>
<td>13.2</td>
<td>16.5</td>
<td>24.8</td>
</tr>
<tr>
<td>10 to 12</td>
<td>12.1</td>
<td>12.9</td>
<td>16.1</td>
<td>24.1</td>
</tr>
<tr>
<td>13 to 17</td>
<td>11.8</td>
<td>12.6</td>
<td>15.7</td>
<td>23.5</td>
</tr>
<tr>
<td>18 to 24</td>
<td>11.6</td>
<td>12.3</td>
<td>15.4</td>
<td>23.1</td>
</tr>
</tbody>
</table>

### Table 2. Decay correction factors – November 2012 to February 2013

<table>
<thead>
<tr>
<th>Date</th>
<th>Factor</th>
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<tbody>
<tr>
<td>14 November 2012</td>
<td>1.048</td>
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<tr>
<td>21 November 2012</td>
<td>1.119</td>
</tr>
<tr>
<td>28 November 2012</td>
<td>1.195</td>
</tr>
<tr>
<td>05 December 2012</td>
<td>1.276</td>
</tr>
<tr>
<td>12 December 2012</td>
<td>1.363</td>
</tr>
</tbody>
</table>

**Time per dwell**

=14.6 * 1.363

=19.9s
Case

- 42 yo man
- PT2a N2 R0 adenocarcinoma – LUL lobectomy 6/2016. extra capsular spread at stations 5 & 10
- EGFR, ALK-1 neg
- adjuvant chemo completed 8/2016
- declined participation into LUNGART trial
Case

• Recurrence 11/2017
• Airway debulking 12/2017
• referred to med onc for palliative systemic therapy options, ? immunotherapy trial.
• PS 1. PDL-1 95% TPS
• Abdominal and shoulder skin mets rapid evolution
Options?

1. Pembrolizumab
2. Clinical trial
3. Palliative RT
4. More airway debulking
5. Gemcitabine/ carboplatin
Case

- ILT attempt 1/2018 failed. Central occlusive disease
- Referred airway debulking
- Died 2 weeks later before could be debulked.
- CXR- cannonball mets
Case Studies
Twin Line Treatments

- Used to treat adjacent lengths of airway
- Bronchoscopy procedure as per single lines.
- A RMW is placed in each catheter, with different markings to enable distinction.
3D Planning

- 3D brachytherapy planning system
• The catheters are reconstructed on the CT scan and the clinician marks the distal and proximal extent of the treatment for each line.
Airway MDT

- tertiary service for pre-treated patients:
  - Recurrence vs fibrosis
  - Biopsies for genetic testing or trials
  - Washings for infection
- ‘medical airway team’ to complement surgical airway team
  - combined specialist input of radiation oncologist and resp medicine, with technical physics team
Fluorescence Bronchoscopy

• Dysplasia, CIS, and microinvasive ca – fluoresce differently when exposed to approp wavelength light – this difference can be detected

• Varying reports on specificity / sensitivity, needs validation
1) Left upper lobe segmentectomy for PT1a N0 NSCLC 9/14

2) RLL apical segment squamous cell ca radical ILT 11/14

3) Post radiation ulcer in RBI
Centre devices

- balloons, cages, or sheaths, can be employed to maintain the radioactive source within the centre of the bronchial lumen and avoid dose inhomogeneity
Summary

• Consider ILT for patients with symptomatic endo-luminal disease

• Palliatively:
  adjunct to chemo
  +/- EXBRT
  following surgical airway Mx
  relapse following previous chemo/ RT

• Radically:
  early stage/ CIS limited to airway
  as prelude to EXBRT if collapse
  ? For +ve bronchial RM
  ?? For non-resectable carcinoid
Summary

indication

- located in trachea, MB or LL (accessible)
- intrinsic tumour essential, some extrinsic compression and submucosal infiltration
- Lumen wide enough to accept catheter
- Survival expected >3 months

Relative contra-indication

- High grade airway obstruction
- Close proximity to large BV/ invasion
- Destruction of bronchial wall/ fistulation
- Unfit for bronchoscopy
WE WANT YOU!

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**Acknowledgements**

- Dr Phil Barber (consultant resp physician)
- Dr Phil Crosbie (consultant resp physician)
- Laura Lane (lead brachy radiographer)
- The Brachytherapy team