The sense and non-sense of radiotherapy and radiofrequency ablation to control isolated lung metastases

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Bone or Soft Tissue Sarcoma

first presentation with metastatic disease

Oligometastatic disease

Chemotherapy
Surgery
RFA
SBRT

Surveillance

Oligometastatic disease

metastatic disease

Chemotherapy
Surgery
RFA
RT/ SABR

40-60% develop metastatic disease of which 70-80% limited to the lungs

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Define oligometastatic disease

1. Oligometastatic disease is an intermediate state of cancer spread between localised disease and widespread metastatic disease

2. The metastases are limited to a single or limited number of organs or number of lesions <5

3. Patients with oligometastatic disease may be amenable to a curative therapeutic strategy

*Hellman and Weischselbaum, 1995*
Selecting patients for a ‘curative’ strategy

Bone or Soft Tissue Sarcoma

1. Disease free interval
   first presentation with metastatic disease

2. Biological behaviour of disease/ histo subtype
   Oligometastatic disease

   Intervention
   Surgery
   SBRT
   RFA

   Surveillance
   Oligometastatic disease

   3. Histological subtype
      metastatic disease
      Chemotherapy
      Surgery
      RFA
      EBRT/ SBRT

   Surveillance
   Oligometastatic disease
   metastatic disease
Indications for radiofrequency ablation (RFA)

1. Maximum number of lesions for one RFA session~3

2. Maximum size of lesion~4-5cm

3. Location:
   i. avoid lesions <1cm from hilum, large vessel, main bronchus, oesophagus or trachea or
   ii. direct contact with vessels ≥3mm diameter or myocardium

4. Path of needle tract must avoid
   Large vessels
   Bronchi
   Blebs
   Fissures

Procedure

1. Sedation/anaesthesia
2. CT fluoroscopy
3. ~12-25 minutes
4. Chest drain if pneumothorax>3cm
Radiofrequency ablation

Insertion of needle
Deployment of tines
RFA at 100°C/25 min

45-50°C: Protein denaturation & loss of cell structure

70°C: Thermal coagulation

100°C: Tissue desiccation & necrosis
A: pre-ablation
B: 1 month post ablation
C: 3 months post ablation
D: 6 months ablation
E: 12 months post ablation
Other forms of thermal ablation

1. cryoablation

2. microwave ablation

3. laser interstitial tumour therapy
stereotactic ablative body radiotherapy (SABR)/SBRT

Highly conformal RT, delivering RT via 100 fine pencil beams to treat a lesion measures <6cm diameter

Treatment takes 1 hour

Much more focussed on the tumour hence less dose to normal tissues
Tracks the tumour during treatment hence less chance of a ‘miss’

Large ablative doses: 40-50 Gy
1. 3#
2. 5#
3. 10# (especially if lesion within 2cm of the central no fly zone)

EQD2 (equivalent dose at 2 Gy/#: can be from 60Gy to 140-200 Gy)
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Indications for stereotactic ablative body radiotherapy (SABR)/SBRT

1. Lesions <6cm in size
2. Commonly when lesions are not amenable to metastasectomy or RFA
3. Lesion amenable to tracking, eg fiducial markers or respiratory gating

Checklist
1. Lung function tests
2. Insertion of fiducial markers
3. Planning CT scan
4. Funding!
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Response assessment after SBRT

Pre SBRT CT (a) shows a left upper lobe lesion, which 5 months post SBRT became more ground glass opacified (b) and 9 months later (c) it demonstrated the orbit sign’ characterized by the presence of a central lesion surrounded by an inner zone of relatively spared lung and an outer zone of ground-glass opacification or consolidation.

Khanda ESR, 2014
But do these local therapies offer improved outcomes....

- Progression free survival
- Overall survival
- Where’s the evidence?
### Radiofrequency Ablation

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Number of metastases</th>
<th>Median follow up</th>
<th>PFS</th>
<th>OS</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakamura 2009</td>
<td>20 (80% received chemotherapy) (55% previous surgery)</td>
<td>89</td>
<td>2002-2007 18 months</td>
<td>NR but 54% developed further lung metastases</td>
<td>3 yr: 29% Complete ablation significant prognostic factor</td>
<td>Pneumothorax: 65% Chest drain: 38%</td>
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<tr>
<td>Pennathur 2009</td>
<td>22 (23% previous surgery) (18% sarcoma)</td>
<td>27</td>
<td>2001-2005 29 months</td>
<td>NR</td>
<td>Est 2 yr: 68%</td>
<td>Pneumothorax: 70%</td>
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<tr>
<td>Palussiere 2011</td>
<td>29</td>
<td>47</td>
<td>2002-2009 50 months</td>
<td>DFS : 7 months (3.5-10)</td>
<td>3yr: 65%</td>
<td>Pneumothorax: 69%</td>
</tr>
<tr>
<td>Von Meyenfeldt 2011</td>
<td>46 (26% sarcoma (78% previous surgery)</td>
<td>90</td>
<td>2004-2009 22 months</td>
<td>2 yr: ~22%</td>
<td>3yr:~ 69%</td>
<td>Pneumothorax 34% Chest drain 25%</td>
</tr>
<tr>
<td>Koelbinger 2014</td>
<td>22</td>
<td>55</td>
<td>2007-2012 20 months</td>
<td>2 yr: 23%</td>
<td>3yr: 85% Disease free interval impacted on OS</td>
<td>Grade 3 toxicity: 7%</td>
</tr>
</tbody>
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## Stereotactic Ablative Body Radiotherapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Number of metastases</th>
<th>Median follow up</th>
<th>PFS</th>
<th>OS</th>
<th>Dose delivered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stragliotto 2012</td>
<td>46</td>
<td>136 (97 lung)</td>
<td>1994-2005</td>
<td>2 yr local control 90%</td>
<td>3 yr: 34%</td>
<td>20 Gy/1#</td>
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<td></td>
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<td></td>
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<td>24 -45 Gy/3#</td>
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<td>24-48 Gy/4#</td>
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<td></td>
<td>20-40 Gy/5#</td>
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<tr>
<td>Dhakal 2012</td>
<td>52 SBRT</td>
<td>74</td>
<td>1990-2006</td>
<td>3yr local control : 82%</td>
<td>Median OS: 2yrs</td>
<td>50 Gy/5#</td>
</tr>
<tr>
<td>Mehta 2013</td>
<td>16 SBRT</td>
<td>25</td>
<td>2009-2011</td>
<td>nr</td>
<td>4yr: 72%</td>
<td>54 Gy/3#</td>
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<td>50 Gy/4#</td>
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<td>36 Gy/3#</td>
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<td>42 Gy/3#</td>
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<tr>
<td>Singh 2014</td>
<td>34 (4 sarcoma)</td>
<td>49</td>
<td>2008-2011</td>
<td>nr</td>
<td>2yr: 44%</td>
<td>40 Gy/5#</td>
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<td></td>
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<td></td>
<td>3yr local control : 82%</td>
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<td>45 Gy/5#</td>
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<td></td>
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<td></td>
<td>50 Gy/5#</td>
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<td></td>
<td></td>
<td></td>
<td>60 Gy/5#</td>
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<tr>
<td>Soyfer 2014</td>
<td>22</td>
<td>53</td>
<td>95 months</td>
<td>nr</td>
<td>5yr: 62%</td>
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<tr>
<td>Merrell 2014</td>
<td>21 (50% lung)</td>
<td>30</td>
<td>2008-2013</td>
<td>nr</td>
<td>2yr: 58%</td>
<td>50Gy/5#</td>
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<td>4yr: 12.5%</td>
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**Current studies:**

NCT01949506: SBRT and ART for pulmonary metastases from soft tissue sarcoma, N=20, 1-5 mets, <5cm

**Primary endpoint:** acute toxicities from SBRT

**Secondary endpoints:** local control, disease free survival, overall survival, quality of life
Estimated 5 year overall survival for STS:

- All cases: 15%\(^1\)
- Pulmonary metastasectomy: 25%\(^2\)
- RFA: 30%\(^3\)
- SABR: ~20%\(^4\)

1. Thames cancer registry 1995-2004
2. Treasure BMJ 2012
3. Nakamura Cancer 2009
4. Dhakal IJROBP 2012
In conclusion

There is sense in considering a non-surgical approach

1. Avoid an operation
2. Low morbidity
3. Minimal collateral lung damage

However...
- there is a selection bias which may make it impossible to determine which is superior?

So ... currently, best practice
1. individualise according to
   - disease free interval
   - histological subtype
   - true oligometastatic disease
2. Discussion in the context a thoracic sarcoma MDT
   - Prospectively collected database of survival outcomes and complications to establish criteria for use of the different treatment modalities
3. Need to establish the evidence to determine impact on PFS and OS
What we really want to know is whether we have a robust decision-making process that delivers consistency, and of course whether our approach is clinically worthwhile at all.....