Radiotherapy (RT) for Upper GI Cancers

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INTRODUCTION

• Role of RT in upper GI cancers
  – radical/adjuvant/palliative
  – oesophagus/stomach/pancreas/hepatobiliary

• Advances in radiotherapy
  – simulation
  – delivery

• Potential side effects
  – acute
  – late
  – management

• Case study
ROLE OF RADIOTHERAPY - RADICAL

• Oesophagus
  – inoperable
  – medical comorbidities

• 5-6 weeks of radiotherapy (1 treatment/day, 5 days/week) with concurrent chemotherapy
ROLE OF RADIOTHERAPY – NEO-ADJUVANT

- Neoadjuvant
  - oesophagus – CROSS (4½ weeks of daily radiotherapy with concurrent chemotherapy)
  - pancreas

<table>
<thead>
<tr>
<th></th>
<th>Neoadjuvant chemoradiotherapy plus surgery (n=178)</th>
<th>Surgery alone (n=188)</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locoregional progression</td>
<td>39 (22%)</td>
<td>72 (38%)</td>
<td>0.45 (0.30-0.66)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Distant progression</td>
<td>70 (39%)</td>
<td>90 (48%)</td>
<td>0.63 (0.46-0.87)</td>
<td>0.0040</td>
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<tr>
<td>Overall progression</td>
<td>87 (49%)</td>
<td>124 (66%)</td>
<td>0.58 (0.44-0.76)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are n (%), unless otherwise indicated. Comparison between treatment groups was based on univariable cause-specific Cox regression modelling of progression-free intervals. Deaths from non-disease-related causes were censored. Overall progression was defined as either locoregional progression or distant progression. Patients with both locoregional disease progression and distant disease progression (22 patients in the neoadjuvant chemoradiotherapy plus surgery group and 38 in the surgery alone group) were counted in both locoregional progression and distant progression categories. HR=hazard ratio.

Table 3: Patients with locoregional or distant progression in the two treatment groups
ROLE OF RADIOTHERAPY - ADJUVANT

- Adjuvant:
  - oesophagus
  - gastric
  - pancreas
  - hepatobiliary
ROLE OF RADIOTHERAPY

• Palliative:
  – any primary site
  – metastases – bone, brain
  – generally shorter course than radical, adjuvant courses – 1 day to 3 weeks
ROLE OF RADIOTHERAPY - PALLIATIVE

- Painful bone metastases:
  - clinical response (partial or complete) in 60-80%
  - complete response in up to 1 in 4
  - delay to full effect can be up to 4-6 weeks post-RT
  - multiple studies showing effectiveness of even a single fraction of RT
  - techniques (eg. VMAT) now able to be used to minimise toxicity

Palliative radiation therapy for bone metastases:
Update of an ASTRO Evidence-Based Guideline

Stephen Lutz MD a,*, Tracy Balboni MD MPH b, Joshua Jones MD c, Simon Lo MB ChB d, Joshua Petit MD e, Shayna E. Rich MD PhD f, Rebecca Wong MB ChB g, Carol Hahn MD h

Radiation therapy continues to be gold standard for palliative care of painful bone metastases

ARLINGTON, Va., February 14, 2017

Updated ASTRO guideline upholds standard of care and emphasizes safety and efficacy of radiation treatment
ROLE OF RADIOTHERAPY - PALLIATIVE

• Brain metastases:
  – whole brain or targeted to visible brain lesions
  – best outcomes for single or small number of metastases

• Primary tumour – bleeding or obstruction:
  – response can take 48-72hrs or longer
  – brachytherapy for obstruction
ADVANCES IN RADIOTHERAPY

• The holy grail of radiotherapy:
  – deliver high dose of radiation to the tumour
  – minimise dose of radiation to normal tissues
ADVANCES IN RADIOTHERAPY – The Radiotherapy Process
ADVANCES IN RADIOTHERAPY - SIMULATION

- CT simulation with contrast, 4DCT
- PET fusion
- Immobilisation – abdominal compression device
- Gating, breathing control devices
ADVANCES IN RADIOTHERAPY - DELIVERY

- 2D – orthogonal films (AP, lateral), basic shielding
- 3DCRT – 3D conformal radiotherapy – multiple fields from all angles, requires 3D imaging
- IMRT – intensity modulated radiotherapy
- VMAT – volumetric modulated arc therapy
ADVANCES IN RADIOTHERAPY - DELIVERY

• IMRT – even more conformal high dose region with quicker dose drop off, but larger volume of normal tissue receives low dose
• VMAT – continuous arc therapy
ADVANCES IN RADIOTHERAPY - DELIVERY

- IGRT – image-guided radiotherapy
- Daily imaging and online treatment table shifts
- Essential for delivery of IMRT/VMAT
IMRT/VMAT vs 2D/3DCRT

ADVANTAGES
- Improved normal tissue sparing
- Reduced toxicity
- Enables dose escalation
- Allows simultaneous integrated boost

DISADVANTAGES
- Contouring time for RO
- More moving parts, so increased risk of errors
- Engineering input and rigorous physics QA needed
- Cost
- Increased risk of geographic miss
- Increased treatment time (IMRT)
- Increased emphasis on patient setup and day-to-day variation
- Increased integral dose to patient
- Larger “low dose wash” ?theoretical increase in 2nd malignancy rates
ADVANCES IN RADIOTHERAPY - SBRT

• Stereotactic body radiotherapy (SBRT) aka stereotactic ablative radiotherapy (SRS)
• Origins in brain lesions/tumours with use of stereotactic radiosurgery (SRS)
• Shift from multiple low dose treatments to small number of high dose treatments
• Intent to ablate or necrose tissue in high dose area
• Requires ultimate level of patient immobilisation, image guidance and tumour tracking
• Not every cancer and every patient will benefit from Cyberknife
• And Cyberknife is only one of a number of techniques to deliver SBRT/SABR
POTENTIAL SIDE EFFECTS - ACUTE

- Side effects during and within 3 months of radiotherapy
- Generally predictable and relatively common
- Fatigue
- Otherwise, side effects of RT are determined by anatomical location of target
- For UGI cancers:
  - oesophagitis
  - N&V, diarrhoea
  - anorexia, wt loss
- Management:
  - anti-emetics – metoclopramide, ondansetron
  - anti-diarrhoeals – loperamide, codeine
  - dexamethasone
  - xylocaine viscous, mylanta/gaviscon
  - systemic analgesia – fentanyl patch, liquid formulations
  - feeding tubes - NGT, RIG, PEG
POTENTIAL SIDE EFFECTS - ACUTE

• Palliative radiotherapy – bone metastases:
  – pain flare – 10-20%
  – fatigue
  – otherwise depends on location of treated bone metastasis, eg. lumbar spine → N&V, thoracic spine → oesophagitis

• Palliative radiotherapy – brain metastases:
  – fatigue
  – alopecia, scalp skin reaction
  – headache
  – N&V
  – late – effects on memory, higher mental functions
POTENTIAL SIDE EFFECTS - LATE

• Side effects beyond 3 months from radiotherapy
• Unpredictable, uncommon and can be difficult to treat
• Pathogenesis related to fibrosis, necrosis, microvascular changes
• For UGI cancers:
  – oesophageal stricture
  – lung fibrosis
  – GI bleeding
  – bowel obstruction, perforation
  – liver/renal failure
  – spinal cord injury
POTENTIAL SIDE EFFECTS – LATE

• Management depends on specific effect:
  – oesophageal stricture - dilation
  – lung fibrosis
  – GI bleeding – endoscopy, measures to reduce bleeding
  – bowel obstruction, perforation - surgery
  – liver/renal failure, spinal cord injury – difficult to manage; fortunately not seen in modern radiation therapy

• Oxpentifylline (Trental)
• Hyperbaric oxygen (HBO)