Recent advances in Radiation Oncology

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Disclosure Information

I have the following financial relationships to disclose:

Stockholder/Co-founder in: Capio Biosciences and Archimmune therapeutics

Research funding from Capio Biosciences

- and -

I will not discuss off label use and/or investigational use in my presentation.
Radiation Oncology

- A key component of cancer treatment
- 60% of cancer patients receive radiotherapy sometime during their illness
- Together with surgery and chemotherapy, radiation is part of the trimodality regimen that treats and cures cancer

UNC Radiation Oncology

- 8 Sites including main campus (UNC Chapel Hill)
- Faculty:
  - 21 physicians
  - 15 physicists
- Capabilities:
  - 12 LINAC machines
  - Cyberknife Radiosurgery
  - Tomotherapy machines
  - HDR brachytherapy
  - LCDR brachytherapy
  - Intraoperative Radiation
Radiation technologies

LINAC

IORT
Oligometastasis

- A condition with a few metastases arising from tumors that have not acquired a potential for widespread metastases
- Potentially curable disease and treatment can bring survival benefit
- Long history of oligometastasis treatment—liver metastasis from colorectal cancer, brain mets from lung cancer
- Challenge: adequate treatment of the oligometastasis
- Solution: stereotactic ablative body radiotherapy
Randomized phase II
- Three or fewer metastases, not including the primary tumour (nodes are counted collectively)
- Randomly assigned (1:1) to either local consolidative therapy (radiotherapy or surgery) with or without maintenance treatment or to maintenance treatment alone
- Single institution randomized phase II
- Maintenance chemotherapy alone vs SAbR followed by maintenance chemotherapy
- Primary plus up to 5 metastatic sites
PFS improvement

Figure 2: Analysis of Progression-Free Survival

Summary

- SABR treatment of oligometastatic disease in NSCLC appears to improve survival
- Similar data in other cancers such as prostate cancer
- SABR is easy to do with limited toxicities
- Cyberknife is an excellent tool for SABR treatment
- Patients with oligometastatic disease should be considered for SABR
  - Less than 5 metastases
  - Indication for oligo-progressive disease is emerging
  - Doing well on systemic therapy with 1 or small number of lesions progressing only
Local radiation for low-volume metastatic prostate cancer

Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

- Randomized phase III at 117 hospitals in Switzerland and UK
- Newly diagnosed metastatic prostate cancer
- 1:1 randomization to standard of care vs. standard of care+local XRT
Summary

• Four or more bone sites outside the vertebrae and pelvis, and/or visceral metastases was considered a high metastatic burden and all other assessed patients classified as low.

• Low metastatic burden PCa patients should be considered for local XRT.

• Patients with locally obstructive symptoms should also be considered for XRT.
ASCEND-RT for high risk prostate cancer

Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (th ASCENDE-RT Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-risk Prostate Cancer

W. James Morris, MD, FRCPC, Scott Tyldesley, MD, FRCPC, Sree Rodda, MBBS, MRCP, FRCR, Ross Halperin, MD, FRCPC, Howard Pai, MD, FRCPC, Michael McKenzie, MD, FRCPC, Graeme Duncan, MB, ChB, FRCPC, Gerard Morton, MB, MRCP, FRCPC, FFRRCSI, Jeremy Hamm, MSC, and Nevin Murray, MD, FRCPC.

Randomization (N=198)  
- Allocated to DE-BRT arm (N=99)  
  - 6 received allocated intervention (patient decision)  
  - 7 received neither intervention (patient decision)  
- Allocated to LR-PB arm (N=99)  
  - 6 received DE-BRT arm (patient decision)  
  - 7 received neither protocol intervention (patient decision)

Allocation

Follow-up (N=198)  
- Case were removed at last follow-up and analyzed actuarially

Analysis

Analysed for disease control endpoints (N=198)  
- Excluded from analysis (N=0)

Analysed for toxicity endpoints (N=195)  
- Excluded from analysis (N=3)  
  - 6 received DE-BRT intervention and 7 received neither intervention
  - Exclusion from LR-PB arm included in toxicity analysis (N=4)

Analysed for toxicity endpoints (N=203)  
- Excluded from analysis (N=0)

Analysed for toxicity endpoints (N=388)  
- Excluded from analysis (N=4)
  - 2 received DE-BRT intervention and 7 received neither intervention
  - Exclusion from LR-PB arm included in toxicity analysis (N=4)
Summary

- Patients with high risk or high intermediate risk PCa should be considered for the ASCEND-RT regimen
- Brachytherapy should be done at a high volume place as quality of brachytherapy is associated with volume
Early salvage radiotherapy for prostate cancer

- RADICALS trials
- Adjuvant vs early salvage RT
- Reported at ESMO—no benefit to adjuvant
- Await publication
- Important: early salvage means PSA >0.1 would trigger treatment

Radiation and cancer immunotherapy

Clinical strategy: Radiation + checkpoint inhibitors
Abscopal effect
Improved antigen exposure
No improvement in antigen presentation


http://www.gnsbio.co.kr/?page_id=217&lang=en

**Table:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>No previous thoracic radiotherapy (n=73)</th>
<th>Previous thoracic radiotherapy (n=24)</th>
<th>p value</th>
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<tr>
<td>All recorded pulmonary toxicities*</td>
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<tr>
<td>Any pulmonary toxicity</td>
<td>29 (40%)</td>
<td>15 (63%)</td>
<td>0.052</td>
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<td>Specific pulmonary toxicities</td>
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<tr>
<td>Dyspnea</td>
<td>15 (21%)</td>
<td>6 (25%)</td>
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<tr>
<td>Cough</td>
<td>16 (22%)</td>
<td>7 (29%)</td>
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<tr>
<td>Wheezing</td>
<td>3 (4%)</td>
<td>1 (4%)</td>
<td>0.99</td>
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<tr>
<td>Pneumonitis</td>
<td>1 (1%)</td>
<td>2 (8%)</td>
<td>0.15</td>
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<tr>
<td>Respiratory failure†</td>
<td>4 (6%)</td>
<td>3 (13%)</td>
<td>0.25</td>
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<td>Grade ≥2 pulmonary toxicity</td>
<td>1 (1%)</td>
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<td>6 (8%)</td>
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<tr>
<td>Pneumonitis</td>
<td>1 (1%)</td>
<td>1 (4%)</td>
<td></td>
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<tr>
<td>Respiratory failure</td>
<td>2 (3%)</td>
<td>3 (13%)</td>
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<td>Treatment-related pulmonary toxicities</td>
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<tr>
<td>Any pulmonary toxicity</td>
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<td>3 (13%)</td>
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<tr>
<td>Specific pulmonary toxicities</td>
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<td>Dyspnea</td>
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<tr>
<td>Pneumonitis</td>
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<td>Grade ≥3 pulmonary toxicity (pneumonitis)</td>
<td>1 (1%)</td>
<td>1 (4%)</td>
<td>0.44</td>
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Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer


Figure 1. Progression-free Survival in the Intention-to-Treat Population.
Shown are Kaplan–Meier curves for progression-free survival (PFS), defined according to the Response Evaluation Criteria in Solid Tumors, version 1.1, and assessed by means of blinded independent central review. Tick marks indicate censored observations, and vertical lines indicate the times of landmark PFS analyses. The intention-to-treat population included all patients who underwent randomization.
Summary

- Radiotherapy is synergistic with cancer immunotherapy
- Growing data on how to apply radiotherapy to improve cancer immunotherapy
- Though higher side effects, patients can remain on immunotherapy while receiving radiation
SBRT for pancreatic cancer

“SBRT” vs. Conventional radiation: What’s the difference?

1. Precision (Higher)
2. Dose (Higher dose per fraction)
3. Volume (Lower)
4. Time (Fewer fractions, more convenient)

How do these factors translate into cancer control and toxicity?
- Potentially better control for smaller tumors
- Risk of severe toxicity if dose or volume are too high

Summary of SBRT evidence – Learning curve

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts</th>
<th>Tx</th>
<th>Med. f/u</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Chang 2009</td>
<td>77 LAPC</td>
<td>25 Gy / 1 fx</td>
<td>12M</td>
<td>1-yr LC: 84% 9% G3 tox (3 ulcers, 3 stricture, 1 perf)</td>
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<tr>
<td>Stanford</td>
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<tr>
<td>Pollom 2014</td>
<td>167 LAPC</td>
<td>25 Gy / 1 fx</td>
<td>8M</td>
<td>1-yr LC: 90% 26% G2 tox with 1 fx 8% G2 tox with 5 fx</td>
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<tr>
<td>Stanford</td>
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<td>25-45 Gy / 5 fx</td>
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<tr>
<td>Comito 2016</td>
<td>45 LAPC</td>
<td>45 Gy / 6 fx</td>
<td>24M</td>
<td>2-yr LC: 87% No G3 toxicity</td>
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<td>Milan, Italy</td>
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<td>Herman 2016</td>
<td>49 LAPC</td>
<td>33 Gy / 5 fx</td>
<td>14M</td>
<td>1-yr LC: 78% 6% G3 tox (1 fistula, 2 bleed)</td>
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<td>Hopkins</td>
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<tr>
<td>Rwigema 2011</td>
<td>71 LAPC</td>
<td>18-25 Gy / 1 fx</td>
<td>13M</td>
<td>1-yr LC: 47% No late toxicity</td>
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<tr>
<td>Pitt</td>
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<tr>
<td>Mahadevan 2011</td>
<td>39 LAPC</td>
<td>24-36 Gy / 3 fx</td>
<td>21M</td>
<td>2-yr LC: 85% 9% G3 tox (bleed, bowel obs)</td>
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<tr>
<td>Harvard</td>
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<tr>
<td>Mellon 2015</td>
<td>110 BRPC</td>
<td>30 Gy / 5 fx</td>
<td>14M</td>
<td>BRPC: 49% R0 resection 7% G3 tox (bleed)</td>
</tr>
<tr>
<td>Moffitt</td>
<td>49 LAPC</td>
<td></td>
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</tbody>
</table>
Celiac plexus SBRT – preliminary results in 21 patients

Results – Primary endpoint

- All patients reported decrease in celiac pain after three weeks
- One third of patients reported pain eliminated entirely by six weeks

Overall summary

- Radiation oncology is an integral part of cancer treatment
- Indications for radiation continue to evolve
- More patients can benefit from radiation treatment with recent updates