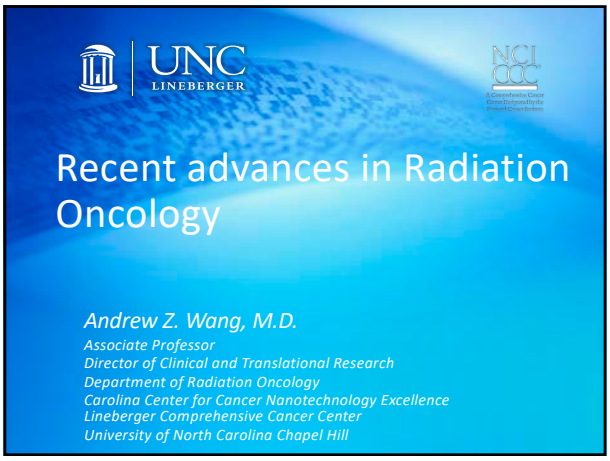
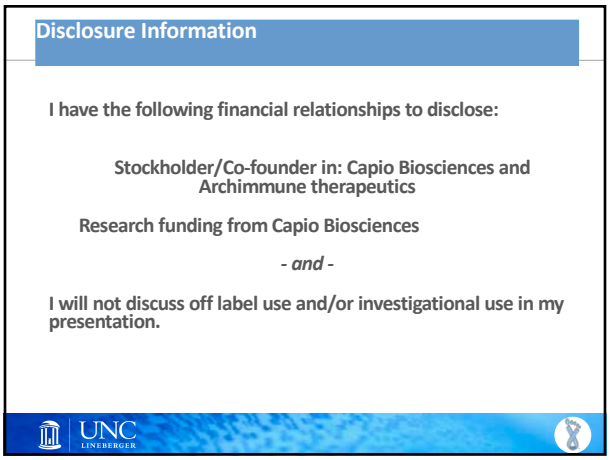

UNC
LINEBERGER
Recent advances in Radiation Oncology
Andrew Z. Wang, M.D.
Associate Professor
Director of Clinical and Translational Research
Department of Radiation Oncology
Carolina Center for Cancer Nanotechnology Excellence
Lineberger Comprehensive Cancer Center
University of North Carolina Chapel Hill

1


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.
UNC

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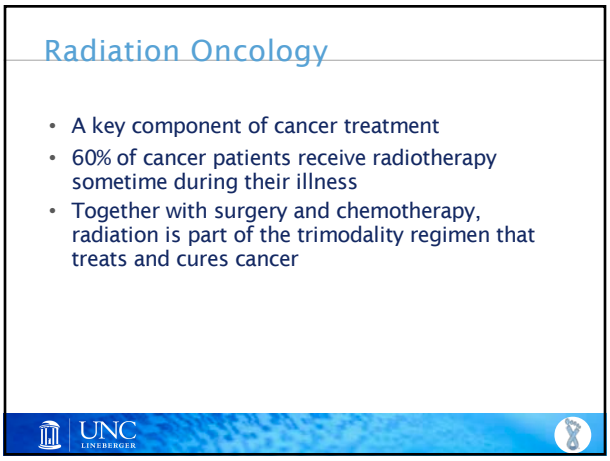
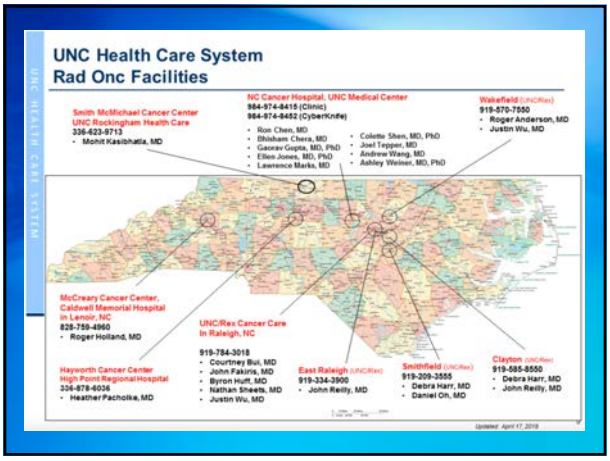

Radiation Oncology
A key component of cancer treatment
60% of cancer patients receive radiotherapy sometime during their illness
Together with surgery and chemotherapy, radiation is part of the trimodality regimen that treats and cures cancer
UNC

3

UNC Radiation Oncology

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

4



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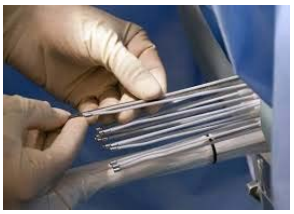
Radiation technologies

LINAC

IORT

6

Cyberknife



Brachytherapy

7

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

8

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

- 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

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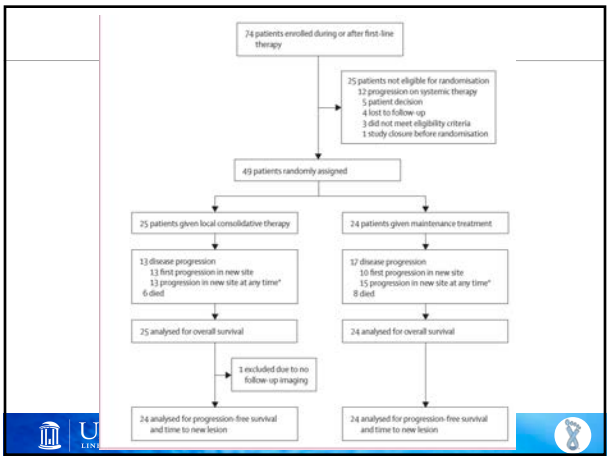

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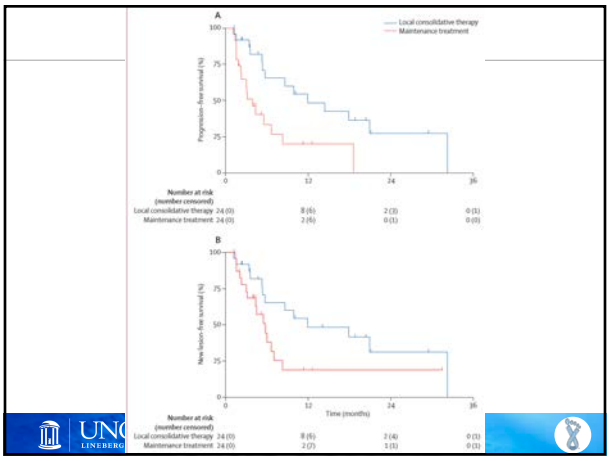

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JAMA Oncology | Original Investigation

Consolidative Radiotherapy for Limited Metastatic Non-Small-Cell Lung Cancer
A Phase 2 Randomized Clinical Trial

Puneeth Iyengar, MD, PhD; Zabi Wardak, MD; David E. Gerber, MD; Vasu Tumati, MD; Chul Ahn, PhD; Randall S. Hughes, MD; Jonathan E. Dowell, MD; Naga Chevella, MD; Lucien Nedzi, MD; Kenneth D. Westover, MD, PhD; Supraldha Pulipparacharuvil, PhD; Hak Choy, MD; Robert D. Timmerman, MD

- Single institution randomized phase II
- Maintenance chemotherapy alone vs SAbR followed by maintenance chemotherapy
- Primary plus up to 5 metastatic sites

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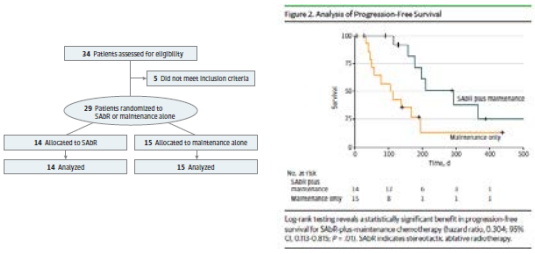
PFS improvement



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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

14

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

Christopher C Parker, Nicholas D James, Christopher D Brawley, Noel W Clarke, Alex P Hoyle, Adnan Ali, Alastair W S Ritchie, Gerhardt Attard, Simon Chowdhury, William Cross, David P Dearnaley, Silke Gillessen, Clare Gilson, Robert J Jones, Ruth E Langley, Zafar I Malik, Malcolm D Mason, David Matheson, Robin Millman, J Martin Russell, George N Thalmann, Claire L Amos, Roberto Alonzi, Amit Bahl, Alison Birtle, Omar Din, Hassan Douis, Chinnamani Eswar, Joanna Gale, Melissa R Gannon, Sai Jonnada, Sara Khaksar, Jason F Lester, Joe M O'Sullivan, Omi A Parikh, Ian D Pedley, Delia M Pudney, Denise J Sheehan, Narayanan Nair Sridhar, Anna T H Tran, Mahesh K B Parmar*, Matthew R Sydes*, on behalf of the Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators†

- 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

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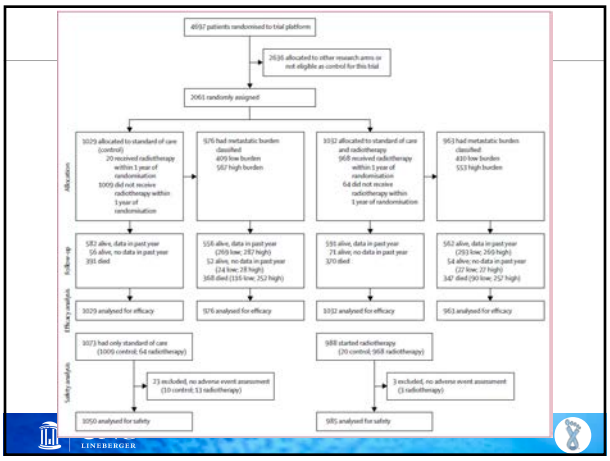

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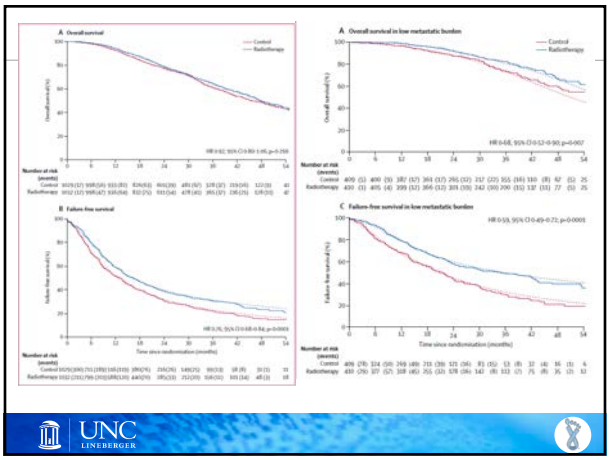

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Summary

- 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

18

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, MRCPI, FRCPC, FFRRCSI,‖ Jeremy Hamm, MSC,¶ and Nevin Murray, MD, FRCPC†,#

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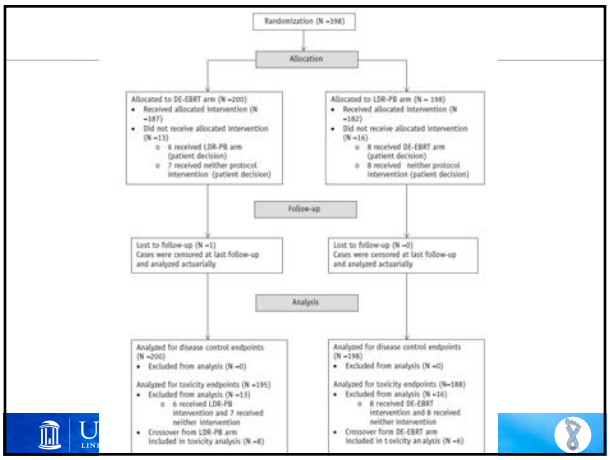

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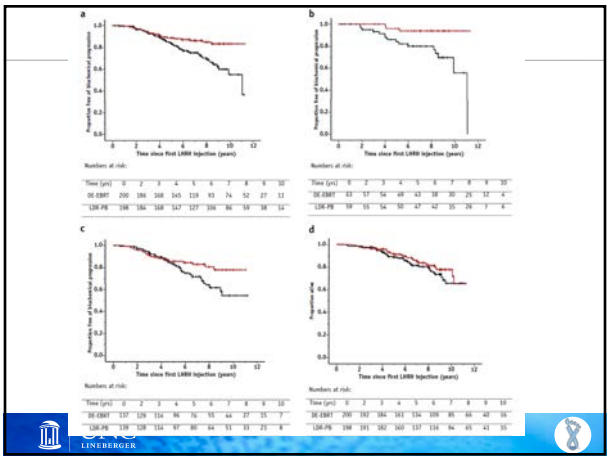

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Summary

- 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

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Early salvage radiotherapy for prostate cancer

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

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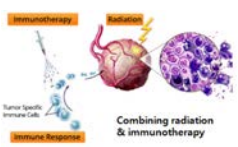
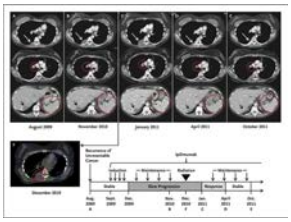
Radiation and cancer immunotherapy

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



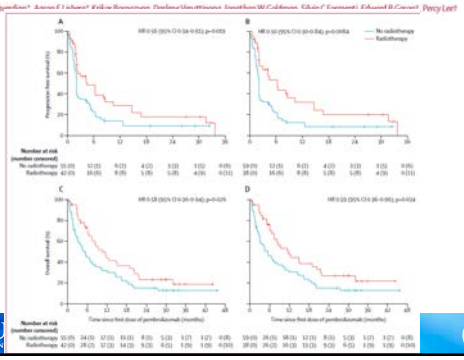


Postow MA et al. N Engl J Med 2012;366:925-931.

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

24

Previous radiotherapy and the clinical activity and toxicity of pembrolizumab in the treatment of non-small-cell lung cancer: a secondary analysis of the KEYNOTE-001 phase 1 trial



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	No previous thoracic radiotherapy (n=73)	Previous thoracic radiotherapy (n=24)	p value
All recorded pulmonary toxicities*			
Any pulmonary toxicity	29 (40%)	15 (63%)	0·052
Specific pulmonary toxicities			
Dyspnoea	15 (21%)	6 (25%)	0·64
Cough	16 (22%)	7 (29%)	0·46
Wheezing	3 (4%)	1 (4%)	0·99
Pneumonitis	1 (1%)	2 (8%)	0·15
Respiratory failure†	4 (6%)	3 (13%)	0·25
Grade ≥3 pulmonary toxicity	9 (12%)	4 (17%)	0·58
Dyspnoea	6 (8%)	0	..
Pneumonitis	1 (1%)	1 (4%)	..
Respiratory failure	2 (3%)	3 (13%)	..
Treatment-related pulmonary toxicities‡			
Any pulmonary toxicity	1 (1%)	3 (13%)	0·046
Specific pulmonary toxicities			
Dyspnoea	0	2 (8%)	0·059
Pneumonitis	1 (1%)	2 (8%)	0·15
Grade ≥3 pulmonary toxicity (pneumonitis)	1 (1%)	1 (4%)	0·44

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 16, 2017 VOL. 377 NO. 20

Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Yokoi, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhail, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Wadsworth, G. Melillo, H. Jiang, Y. Huang, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators*

27

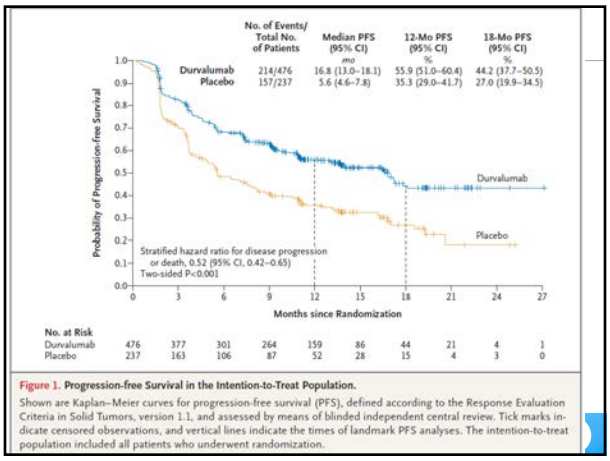

Figure 1. Progression-free Survival in the Intention-to-Treat Population.
Shown are Kaplan–Meier curves for progression-free survival (PFS), defined according to the Response Evaluation Criteria in Solid Tumors, version 1.1, and assessed by means of blinded independent central review. Tick marks indicate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

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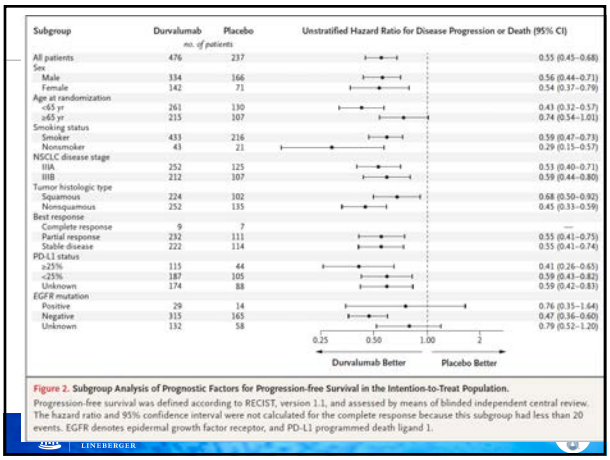

Figure 2. Subgroup Analysis of Prognostic Factors for Progression-free Survival in the Intention-to-Treat Population.
Progression-free survival was defined according to RECIST, version 1.1, and assessed by means of blinded independent central review. The hazard ratio and 95% confidence interval were not calculated for the complete response because this subgroup had less than 20 events. EGFR denotes epidermal growth factor receptor, and PD-L1 programmed death ligand 1.

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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

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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

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Summary of SBRT evidence – Learning curve

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

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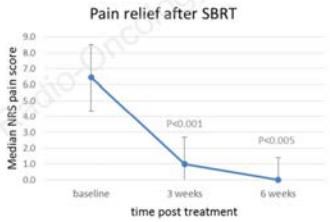
Celiac plexus SBRT – preliminary results in 21 patients

Results – Primary endpoint

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



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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

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