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Physician Perspective on Proton SBRT: Lung and Liver

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NEW YORK PROTON CENTER

Disclosures

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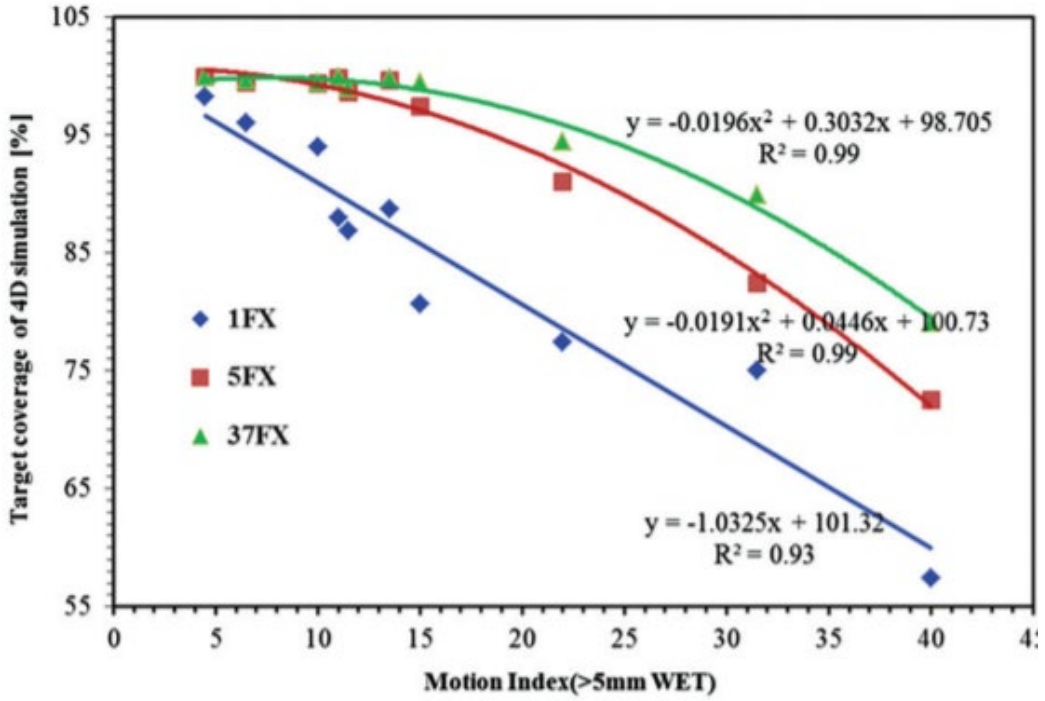
Stereotactic Body Proton Therapy Feasibility

Interplay effect between the target motion and scanning proton spots: can SBRT with protons be delivered in 5 or fewer fractions?

Table 2. Target coverage for the original static plans and 4D simulation of 1, 5 and 37 FXs (standard deviation in parentheses).

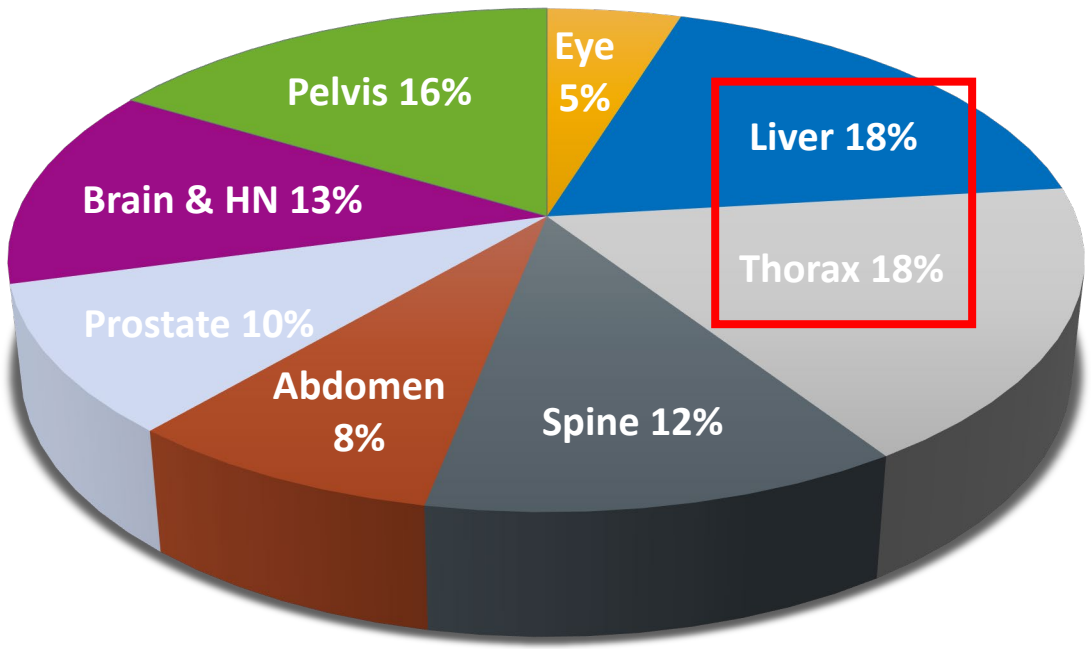
		Coverage [%]			
Patients	MI (>5mm WET)	Static	1 FX	5 FX	37 FX
1	4.5	99.9	98.3 (1.2)	99.9 (0.0)	99.9 (0.0)
2	6.5	99.9	96.0 (0.9)	99.4 (0.3)	99.6 (0.5)
3	10.0	99.7	94.0 (3.1)	99.4 (0.1)	99.5 (0.1)
4	11.0	99.0	88.0 (5.3)	99.8 (0.3)	99.9 (0.3)
5	11.5	99.9	86.9 (4.7)	98.6 (1.1)	99.0 (0.5)
6	13.5	99.8	88.7 (4.3)	99.6 (0.3)	99.9 (0.1)
7	15.0	99.9	80.7 (6.2)	97.5 (1.8)	99.5 (0.9)
8	22.0	100.0	77.4 (5.2)	91.0 (2.1)	94.5 (0.7)
9	31.5	99.0	75.0 (8.4)	82.5 (5.8)	89.9 (0.9)
10	40.0	99.5	57.4 (19.4)	72.6 (12.3)	79.1 (6.2)



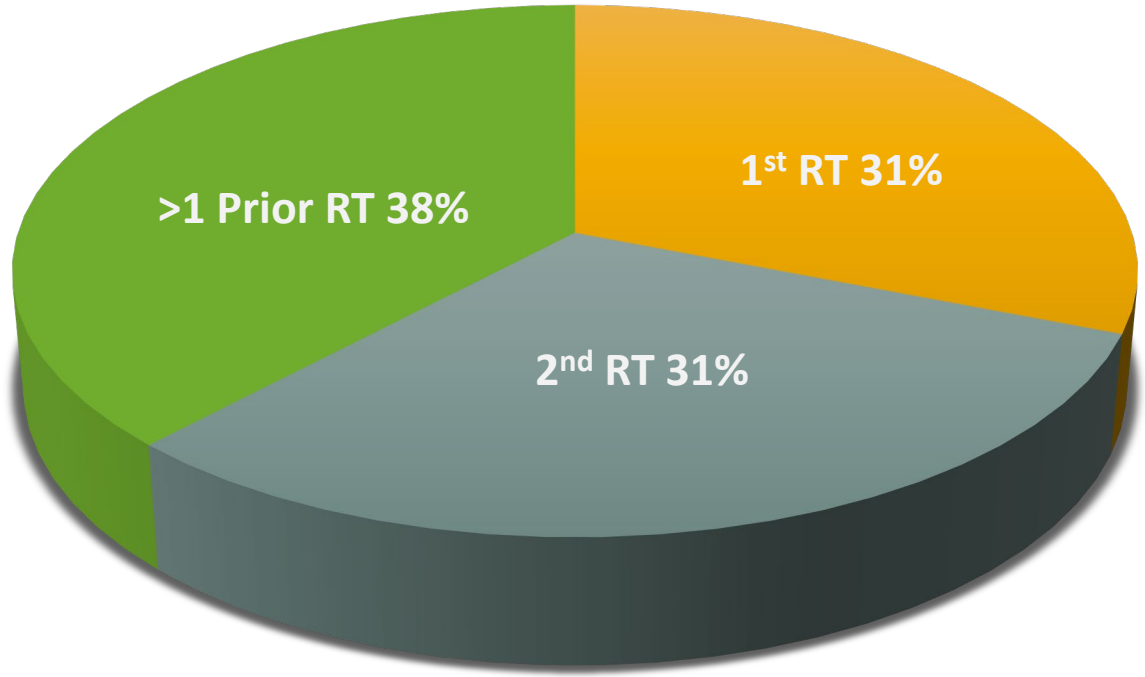
Lin L, Simone CB 2nd, et al. *Med Phys*. 2017;44(2):703-712.

SBRT at NYPC: 8.6% of all Proton Courses (National Avg 0.8%)

SBRT Treatment Diseases at NYPC



Prior RT Status

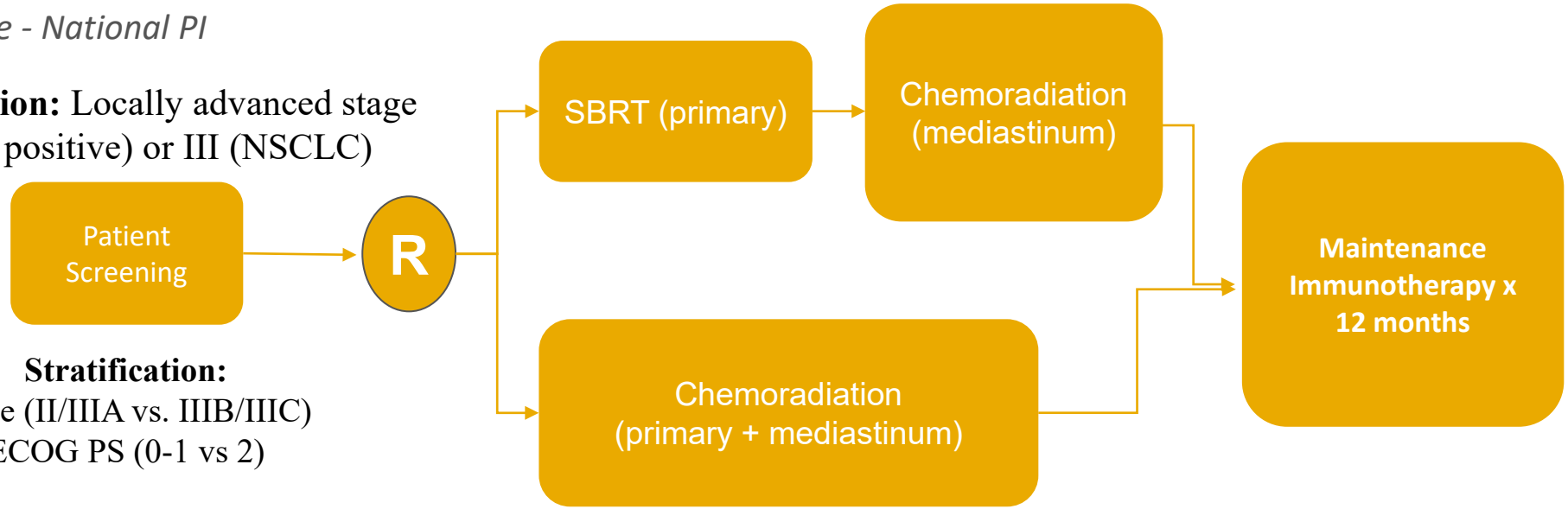


National Data from 2020 NAPT Annual Member Survey

LU008: Phase IIIR Trial of Primary Lung Tumor SBRT Followed by Concurrent Mediastinal Chemoradiation for LA-NSCLC

Charles Simone - National PI

Population: Locally advanced stage II (node positive) or III (NSCLC)

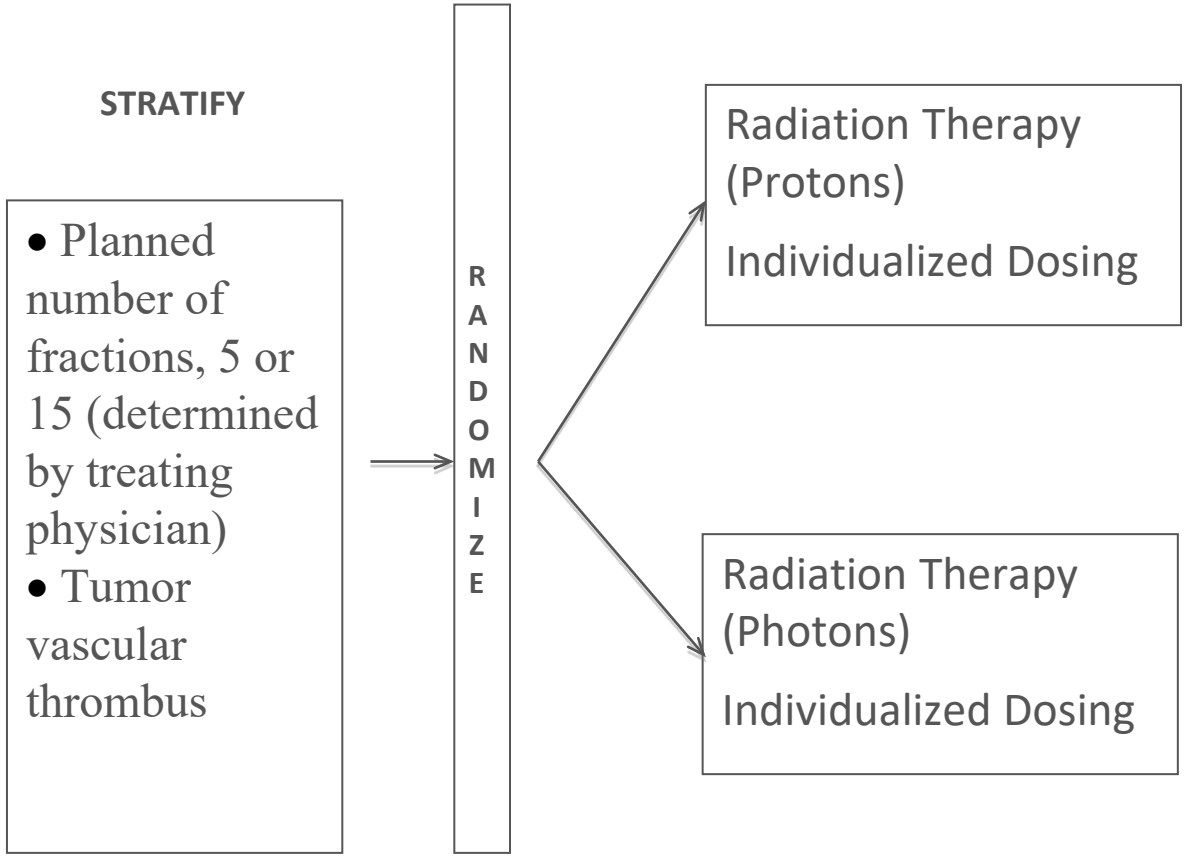


Stratification:
Stage (II/IIIA vs. IIIB/IIIC)
ECOG PS (0-1 vs 2)

- Control arm: chemoradiation to the primary and mediastinal disease (60 Gy/2 Gy) → immunotherapy maintenance x 12 months
- Experimental arm: SBRT to the primary (standard BED ≥100 Gy dose regimen) → chemoradiation to mediastinal disease (60 Gy/2 Gy) → immunotherapy maintenance x 12 months
  - SBRT to primary tumor with photons or protons:
    - 3 fractions to 54 Gy (BED10 of 151.2 Gy) [peripheral]
    - 4 fractions to 50 Gy (BED10 of 112.5 Gy) [peripheral or central]
    - 5 fractions to 50 Gy (BED10 of 100 Gy) [central]
  - Radiation to involved hilar/mediastinal lymph nodes: 2 Gy x 30 fx to 60 Gy, IMRT or proton therapy
  - Concurrent chemotherapy: carboplatin/paclitaxel or cisplatin/etoposide or carboplatin/pemetrexed or cisplatin/pemetrexed
  - Maintenance immunotherapy: durvalumab x 12 months [if durvalumab is NOT given, carbo/paclitaxel pts receive 2 cycles of consolidation]

GI003: A Phase III Randomized Trial of Protons vs. Photons for Hepatocellular Carcinoma

Theodore Hong - National PI



Primary

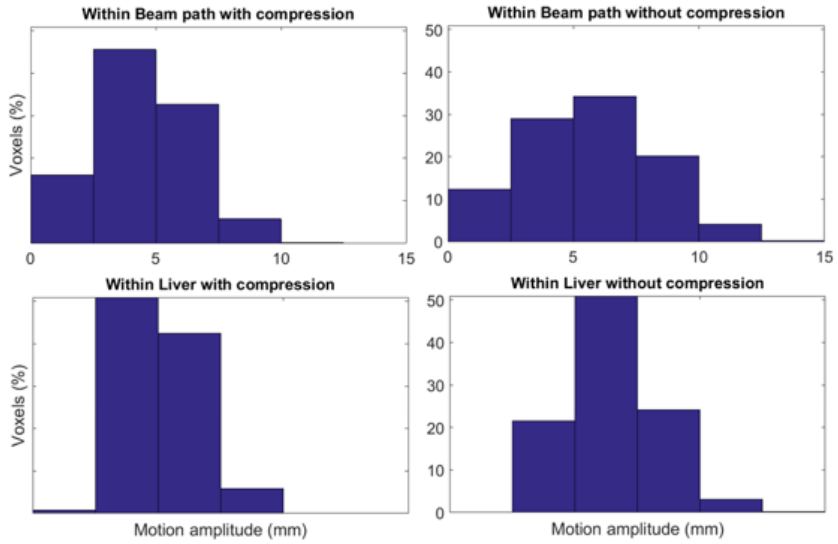
- Overall Survival

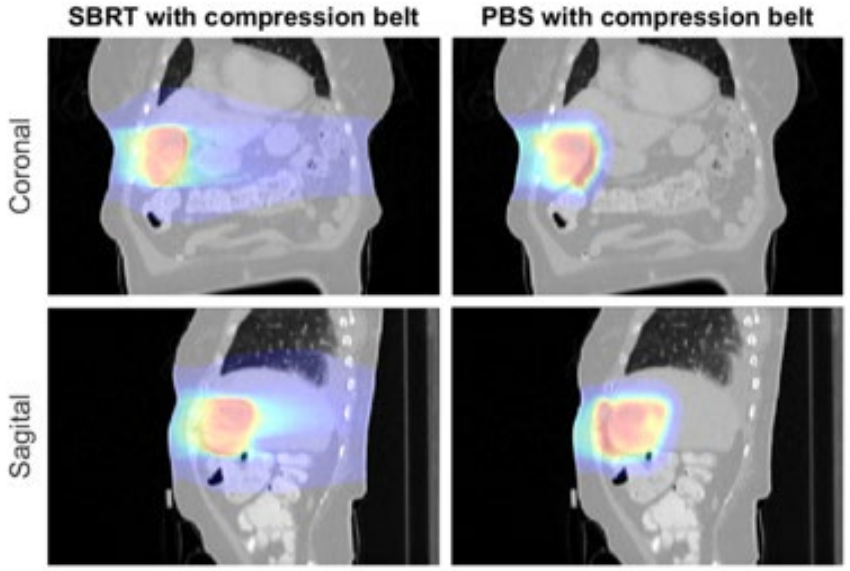
Secondary

- PFS
- LC
- Toxicity
  - Liver function as measured by CP, AlBi
  - PROs (FACT-Hep v.4)

Tumor Motion

- Increased need to account for +/- mitigate motion with protons
- Account for motion from respiration using a 4D sim
- Can mitigate tumor motion with:
  - Breath hold
  - Active breathing control/coaching/biofeedback techniques
  - Forced swallow breathing (commonly abdominal compression)
  - Respiratory gating
  - Dynamic tumor tracking
  - Volumetric repainting
- NYPC Algorithm
  - Thoracic: free breath → compression → SDX
  - Upper GI: compression → SDX





Lin L, Simone CB 2nd, et al. *Med Phys*. 2017;44(2):703-712.

PBS/IMPT SBRT Considerations

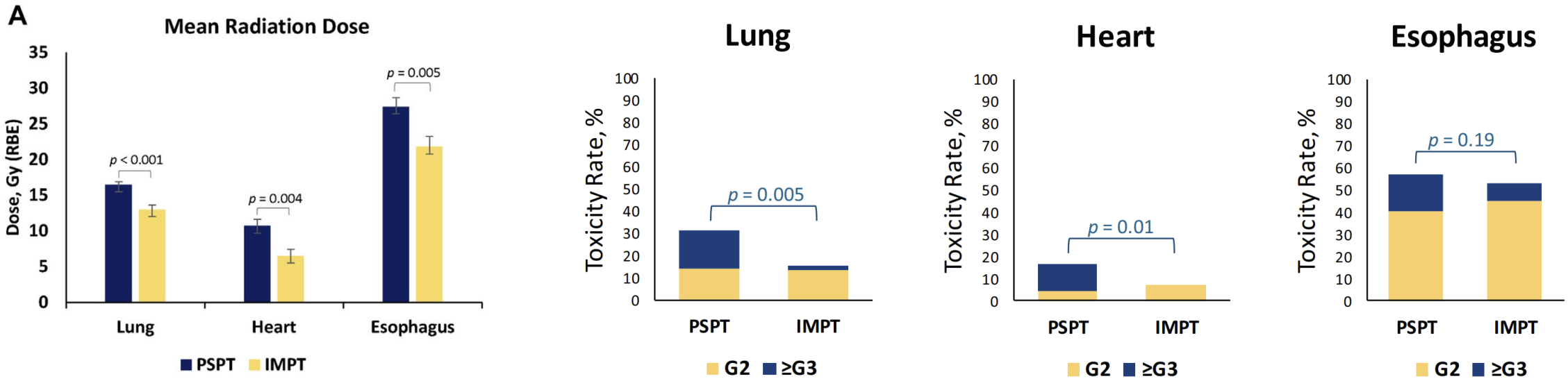
- Double scattering generally only if tumor motion is ≤10 mm
- PBS/IMPT
  - PTCOG Thoracic Subcommittee IMPT Guidelines
    - Rescanning to reduce interplay effects
    - Breath hold, tracking, gaiting, (higher dose rate)
    - In-room volumetric imaging (CBCT), adaptive planning
  - PBS generally only if tumor motion is ≤5 mm or can be mitigated to ≤5 mm
    - Exceptions: reirradiation, significant dosimetric superiority over photon-based SBRT
  - Use CBCT!
- Volumetric Repainting – New York Proton Treatment Center general guidelines
  - ≤ 5 fractions: use volumetric repainting
  - 6-10 fractions: repaint if ≤3 beams, consider if ≥4 beams
  - ≥11 fractions: repainting not routinely used
- Choosing beam arrangements that are robust, minimize uncertainties

Chang JY, Simone CB 2nd, et al. *IJRPOBP*. 2016;95(1):505-16.

Chang JY, Simone CB 2nd, et al. *IJROBP*. 2017;99(1):41-50.

IMPT vs. Passive Scattering Outcomes

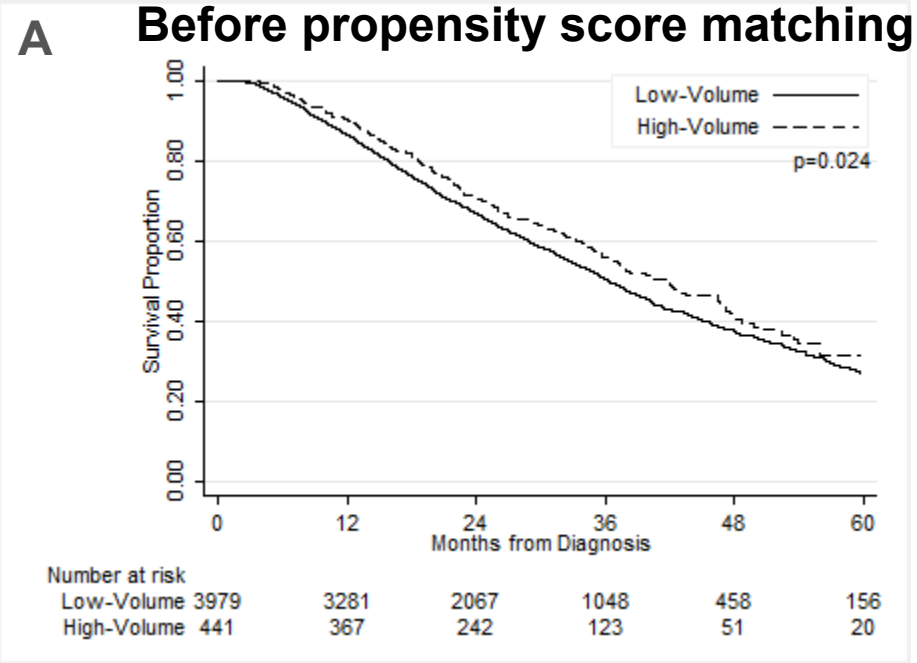
- Nonrandomized comparison of two prospective cohorts of 139 patients with stage II-IIIB and limited stage IV (solitary brain metastasis) treated with concurrent chemotherapy and passive scattering (n=86) or IMPT (n=53)
  - IMPT had lower mean lung (13.0 vs. 16.0 Gy, p<0.001), heart (6.6 vs. 10.7 Gy, p=0.004), and esophagus (21.8 vs. 27.4 Gy, p=0.005) doses
  - IMPT had lower rates of grade ≥3 pulmonary (2% vs. 17%, p=0.005) and cardiac (0% vs. 11%, p=0.01) toxicities
  - IMPT had fewer grade ≥4 toxicities (0% vs. 7%)
  - IMPT had longer median OS (36.2 vs. 23.9 mo, p=0.09)



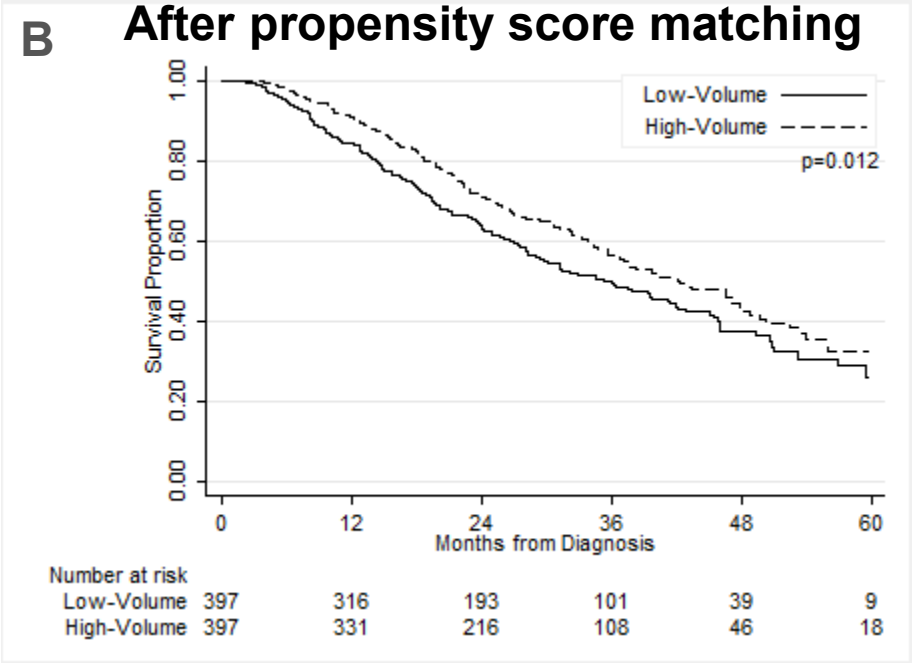
Gjyshi O, et al. *J Thorac Oncol. 2021;16(2):269-277.*

SBRT Results by Center Volume

- NCDB study of cT1-2aN0 NSCLC of 4,420 pts from 2007-2011
  - Variable of interest: facility volume 90th percentile (12 cases/yr)
  - Predictors of treatment at high volume facility: academic center (most associated), race, income, histologic confirmation, BED, tumor size



Median OS 41.9 months at HVF vs. 36.2 months at LVF, p=0.024



For HVF vs. LVF, propensity score-matched HR 0.77 (0.62-0.94), p=0.012

Park HS, et al. ASTRO 2015.

SBRT Results by Center Volume

Sensitivity analysis varying HVF definition

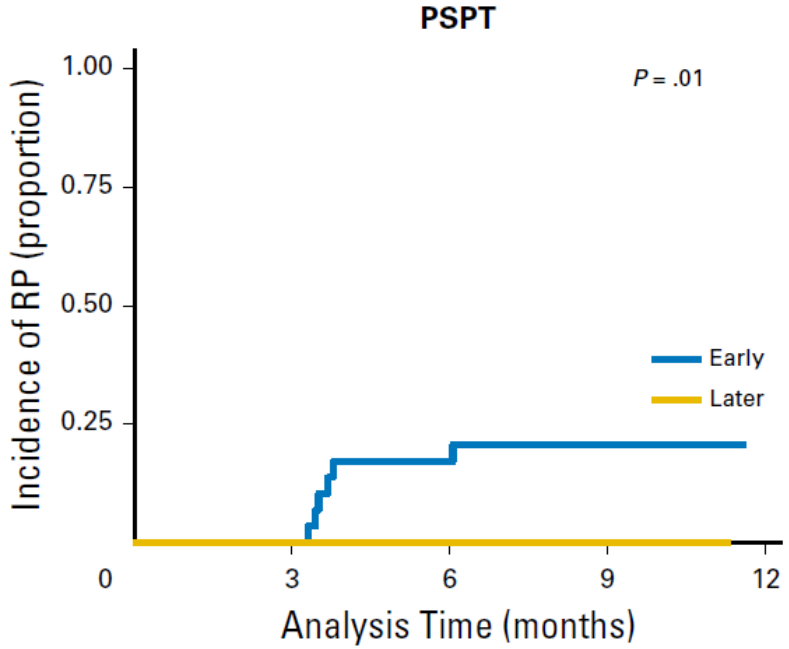
HVF Cut-Off (cases/year)	*Hazard Ratio (95% Confidence Interval)*	*P-value*
6 (59th percentile)	1.01 (0.93-1.10)	0.794
7 (66th percentile)	0.93 (0.85-1.02)	0.112
8 (73rd percentile)	0.91 (0.83-1.01)	0.069
9 (84th percentile)	**0.89 (0.79-0.99)**	**0.039**
10 (87th percentile)	**0.82 (0.72-0.93)**	**0.002**
11 (88th percentile)	**0.81 (0.71-0.92)**	**0.002**
12 (90th percentile)	**0.83 (0.71-0.96)**	**0.014**
13 (90th percentile)	**0.83 (0.71-0.96)**	**0.014**
14 (93rd percentile)	**0.82 (0.71-0.96)**	**0.014**

Conclusion: SBRT at high-volume facilities appears to be independently associated with improved overall survival among clinical stage I NSCLC patients

Park HS, et al. ASTRO 2015.

LA-NSCLC Proton Randomized Data

- MDACC/Harvard Bayesian phase II randomized trial of protons vs. photons
  - Stage II-III NSCLC to 74 Gy with IMRT vs. protons (2 Gy/CGE fx) and concurrent chemo
  - Primary outcomes: grade ≥ 3 radiation pneumonitis or local recurrence within 12 mo
  - Selection bias: of 272 enrolled patients, 149 were randomly allocated to IMRT (n=92) or 3DPT (n=57) [insurance denials, dosimetric differences]
  - Arm imbalances: among randomized patients, proton target volumes were larger (p=0.071) and more patients received higher doses to tumors and had larger lung volumes receiving ≥ 30-80 Gy
  - Failure rates: not significant
  - Pneumonitis rates: not significant
  - Experience matters: combined rate of LF and pneumonitis at 1 year of 31% vs. 13% (p=0.027) if treated in the first or second half of the trial study period



Liao Z, et al. *J Clin Oncol*. 2018;36(18):1813-1822.

National Survey Results

- National practice patterns of proton SBRT for liver and lung tumors conducted by the NRG Proton SBRT Working Group sent to all US proton centers participating in NRG trials in Summer 2021
  - Lung survey results and perspective – Dr. Jeffrey D. Bradley
  - Liver survey results and perspective – Dr. Theodore S. Hong