RadComp

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RADIOTHERAPY COMPARATIVE EFFECTIVENESS

PRAGMATIC PHASE III RANDOMIZED TRIAL OF PROTON VS. PHOTON THERAPY FOR PATIENTS WITH NON-METASTATIC BREAST CANCER RECEIVING COMPREHENSIVE NODAL RADIATION

Health-Related Quality of Life Outcomes

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on behalf of the RadComp Consortium

Introduction

- Radiotherapy plays a major curative role in the treatment of patients with breast cancer
- Proton therapy, by reducing the volume of heart and other tissues exposed to radiation in the treatment of breast cancer, has the potential to lessen the morbidity of radiation therapy compared to photon therapy
- Prior studies have been small, non-randomized, with short follow-up
- Only a large, prospective, pragmatic randomized trial in patients requiring comprehensive radiation can answer these questions

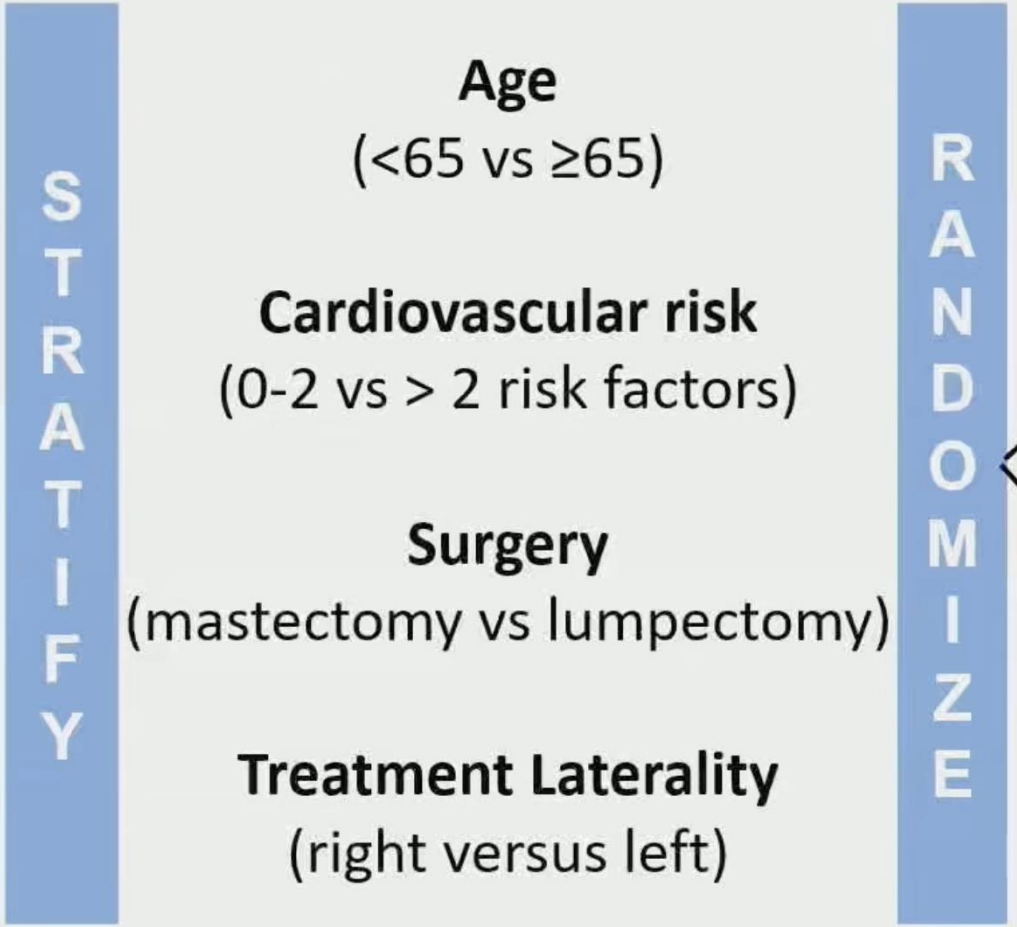
Primary Objective

- To assess the effectiveness of proton vs. photon therapy in reducing major cardiac events (MCE)
- *Primary hypothesis:* For patients with locally advanced breast cancer, proton therapy will reduce the 10-year MCE rate after radiation from 6.3% to 3.8%.
- *Sample size:* 1,238 patients

Secondary Objectives

- To assess the non-inferiority of proton vs. photon therapy in reducing ipsilateral breast cancer local-regional recurrence and in reducing any recurrence
- To assess the effectiveness of proton vs. photon therapy in improving patient-reported body image and function, fatigue, and other measures of health-related quality of life (HRQOL) and adverse events
- To develop predictive models to examine the association of radiation dose distribution to heart and MCE and HRQOL outcomes

RadComp Study Schema



Both arms: Breast/chest wall and nodal radiation with internal mammary node treatment

Dose:45.0 Gy(RBE) to 50.4 Gy(RBE) in 1.8 to 2.0 Gy(RBE) fractions with or without a tumor bed boost

Key Eligibility Criteria

Inclusion

- Invasive mammary carcinoma of the breast
- Non-metastatic or locally recurrent
- Mastectomy or lumpectomy with any axillary surgery or sampling
- Left- or right-sided
- Proceeding with comprehensive nodal radiation with the inclusion of the internal mammary nodes

Exclusion

- Prior radiotherapy to the ipsilateral breast or chest wall
  - Patients with prior contralateral radiotherapy are eligible
- Scleroderma

Methods- HRQOL

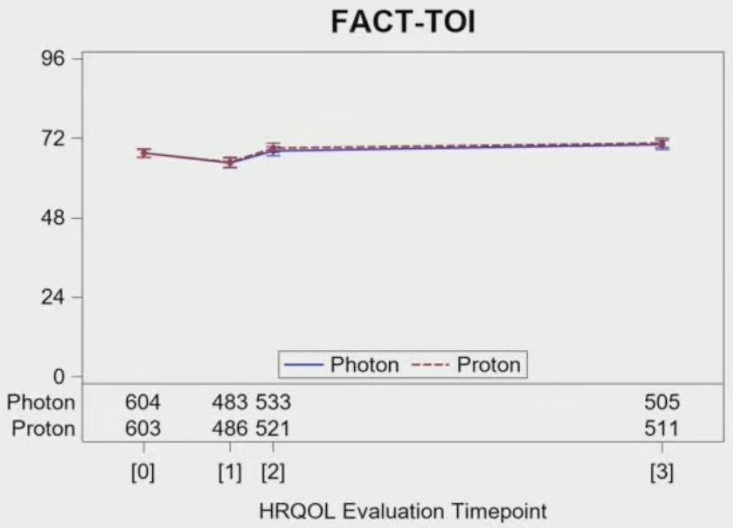
- Primary HRQOL endpoints
  - PROMIS Fatigue, Satisfaction with Breast Cosmetic Outcomes, BREAST-Q adverse effects of radiotherapy, and FACT-B general &breast cancer specific QOL
- Secondary HRQOL endpoints
  - FACIT-TS-G (effectiveness of treatment, treatment was right for me, willingness to recommend treatment, willingness to choose treatment again, satisfaction with the effects, side effects were as expected)
  - PRO-CTCAE (severity, interference, frequency of chest pain, and shortness of breath)

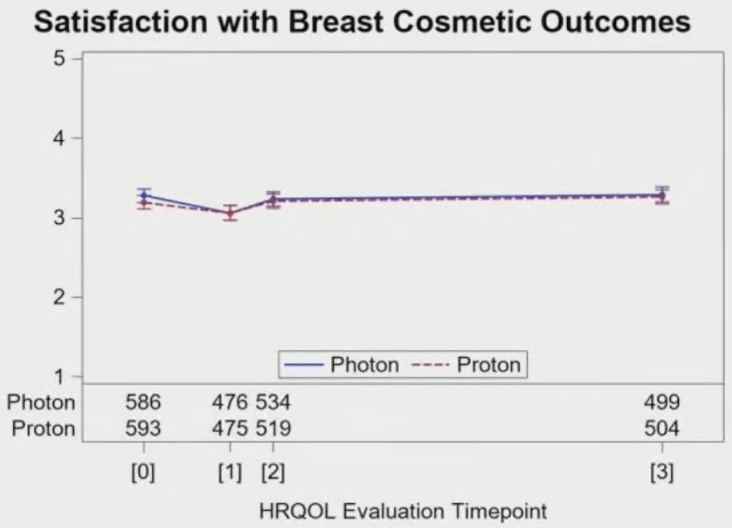
Methods- HRQOL

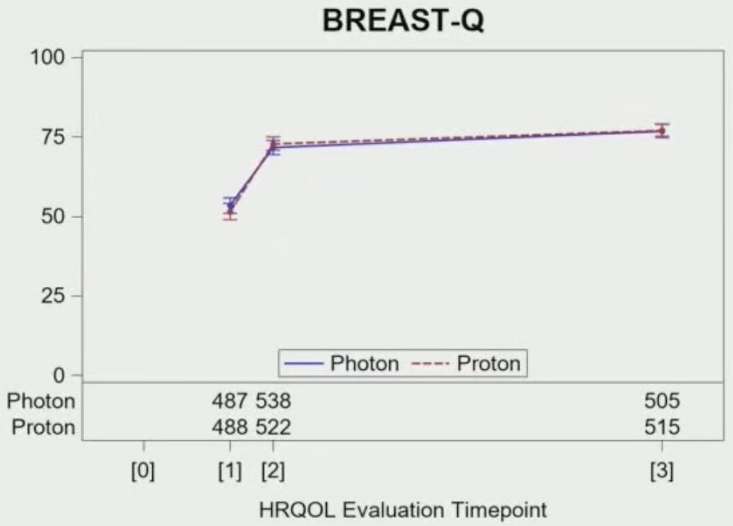
- HRQOL collected at baseline, end of RT, and 1- and 6-month post-RT
- HRQOL measures previously validated in RadComp
- Repeated measures linear and generalized linear mixed models were used to compare the impact of treatment on continuous and ordinal/binary HRQOL scores
- Sufficient power to detect clinically meaningful differences in HRQOL, defined by an effect size >0.33 in mixed-effects models assuming a correlation of 0.40 or higher

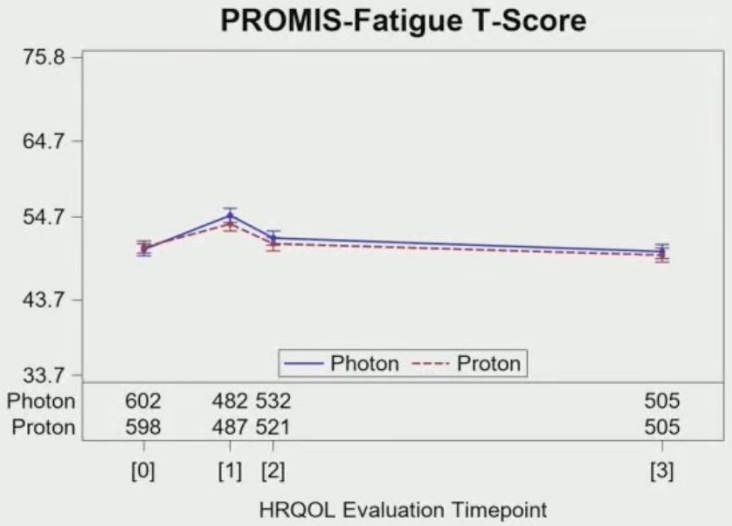
Results

- There were no clinically meaningful differences by treatment arm in:
  - PROMIS Fatigue total score
  - Satisfaction with Breast Cosmetic Outcomes score
  - BREAST-Q total score
  - FACT-B trial outcome index score





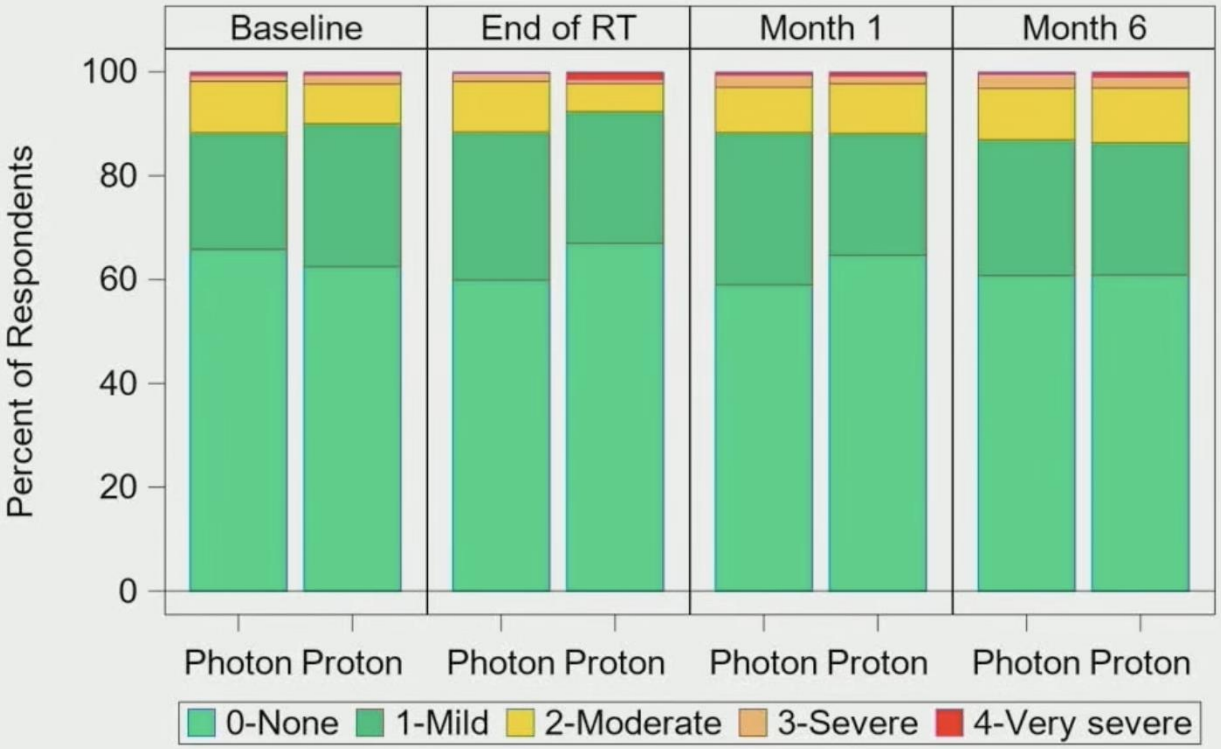




[0]=Baseline, [1]=End of RT, [2]=Month 1, [3]=Month 6

Results

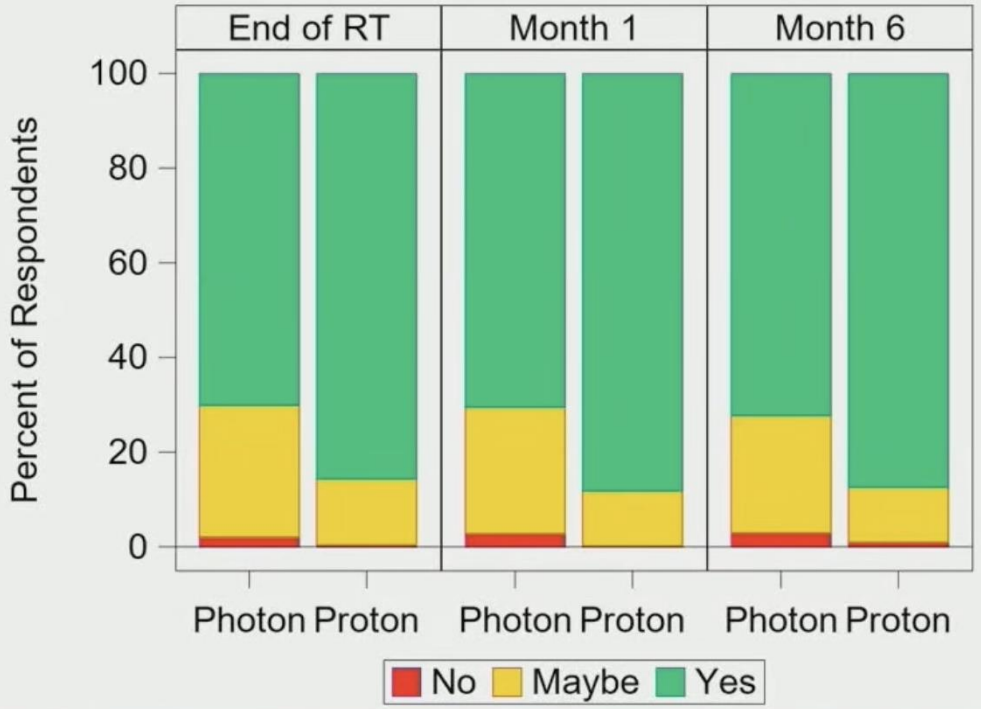
- PRO-CTCAE severity of shortness of breath, when categorized as 0 vs 1-4, significantly favored protons
  - OR=0.74, 95% CI: 0.59-0.93
  - There was no significant difference when categorized as 0-2 vs 3-4
- To address the risk of a false positive, multiplicity analyses were performed and no PRO-CTCAE items retained significance



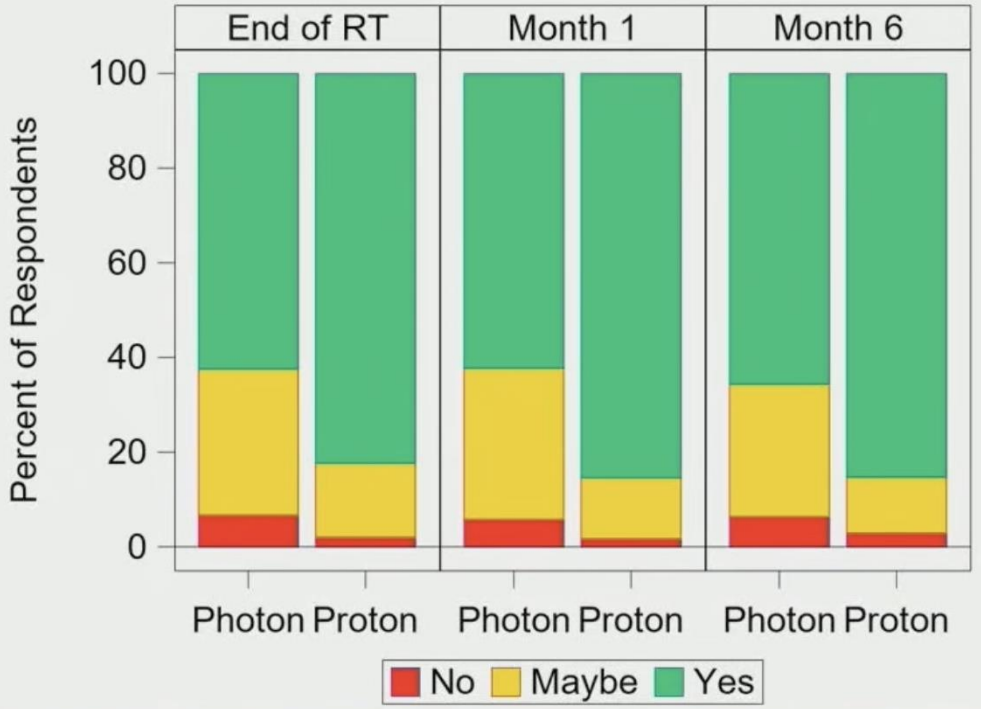
Results

- Five FACIT items were statistically significant in favor of protons including willingness to recommend treatment OR=0.13, 95% CI: 0.08-0.22, p<0.001 or choose treatment again OR=0.11, 95% CI: 0.07-0.18, p<0.001 ;maintained significance after multiplicity analyses

Willingness to Recommend Treatment



Would Choose Treatment Again



Conclusions

- In the first randomized study comparing proton to photon radiation for breast cancer, HRQOL was excellent and similar between treatment arms through 6 months
- Differences favoring protons were noted for FACIT items
  - These must be interpreted in the context of an unblinded study
- Loco-regional control and major cardiac events will be reported according to the study's statistical plan in the future

Thank you!

MedStar Georgetown University Hospital

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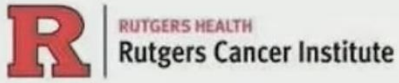

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