**A Meta-Analysis of Randomized Trials to Compare the Added Benefit of a Brachytherapy Boost Versus the Addition of Androgen Deprivation Therapy to External Beam Radiation Therapy in Men with Intermediate and High Risk Prostate Cancer**

W.C. Jackson, R.T. Dess, P.D. Soni, P.W. McLaughlin, and D.E. Spratt;

*Department of Radiation Oncology, University of Michigan, Ann Arbor, MI*

**Purpose/Objective(s):** The strongest independent factor in population registry data for omission of androgen deprivation therapy (ADT) in men receiving radiation therapy is treatment with brachytherapy (BT). This is despite the fact that ADT has been demonstrated to improve distant metastasis-free survival (DMFS) and overall survival (OS) in randomized trials treating with external beam radiation therapy (EBRT), whereas the addition of a BT boost has not. Given this discrepancy between clinical practice and level 1 evidence, we sought to perform a meta-analysis comparing the benefits of the addition of ADT versus BT in intermediate and high-risk prostate cancer.

**Materials/Methods:** MEDLINE and clinicaltrials.gov databases were searched for phase III randomized trials investigating the oncologic benefit of adding ADT to either conventional or dose-escalated EBRT versus addition of BT with or without ADT to EBRT. Included trials were required to report biochemical-recurrence free survival (BRFS) and OS. Meta-analyses were performed with random-effect modeling, and extent of heterogeneity between studies was determined with the Cochran Q and I(2) tests. Pooled hazard ratios (HR) were determined for each endpoint for the addition of ADT vs addition of BT. A model was created based on the different pooled HR to calculate the absolute potential benefit from the addition of ADT or BT based on a patient’s baseline risk of death.

**Results:** In total, 6 trials with 4,663 men met inclusion criteria for comparison of EBRT +/- ADT (RTOG 8610, EORTC 22863, RTOG 9408, DFCI 95096, TROG 9601, EORTC 2291), and 3 trials with 718 men for EBRT +/- BT (ASCENDE-RT, Ontario, UK). Nearly all men had intermediate to high risk prostate cancer. Addition of ADT or BT resulted in similar improvement in BRFS (ADT HR: 0.53 [95%CI 0.48-0.58], BT HR: 0.51 [95%CI 0.36-0.73]). For DMFS the addition of ADT significantly improved DMFS (HR 0.67 [95%CI 0.54-0.83]) while the addition of BT did not (HR: 0.83 [95%CI 0.50-1.38]). Similarly, adding ADT to EBRT significantly improved OS (HR 0.74 [95%CI 0.64-0.86]), whereas the addition of BT did not (HR: 0.97 [95%CI 0.72-1.31]). Estimated improvements in 10-year OS based on underlying risk of death for the addition of ADT or BT are in Table 1.

**Conclusion:** The addition of either ADT or BT to EBRT similarly improves BRFS in men with intermediate to high risk prostate cancer. Conversely, the addition of ADT significantly improves DMFS and OS by 20-30%, whereas addition of a BT boost does not. In absence of a randomized trial showing otherwise, the addition of a BT to EBRT should not replace ADT, and ADT should be given with BT for unfavorable intermediate and high-risk prostate cancer.