Conclusion: For ESCC patients (stage T3-4, any N, M0) undergone esophagectomy, postoperative radiotherapy with small field had similar survival outcome (OS and PFS) with large field radiation. However, patients received small field radiation had much more locoregional recurrence and worse LPFS than patients with large field radiation. A large field postoperative radiotherapy may improve the locoregional control rate for ESCC patients.

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A Randomized Phase II Trial of Neoadjuvant Chemotherapy Compared With Chemoradiation Therapy in Locally Advanced Gastroesophageal and Gastric Adenocarcinoma: Preliminary Results

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Purpose/Objective(s): Whether the addition of neoadjuvant chemoradiotherapy (NACRT) to surgery can improve outcomes better than neoadjuvant chemotherapy (NACT) followed by surgery is not clear. This phase II study was designed to evaluate whether NACRT was superior to NACT with both followed by surgery and postoperative chemotherapy for locally advanced gastroesophageal and gastric adenocarcinoma.

Materials/Methods: Patients with resectable or unresectable gastric cancer (cT3-c4N0M0 or cT3N2-M0) were randomized to either NACT or NACRT arm in a 1:1 ratio with stratification by clinical T stage (cT1-3 vs cT4). NACT arm consisted of three cycles of SOX (S1-40 to 60 mg, orally twice daily on days 1 to 14, oxaliplatin 130 mg/m2 intravenously on day 1, 21 days per cycle followed by radical surgery and another postoperative cycle of SOX. NACRT arm received intensity-modulated radiotherapy with a simultaneous integrated boost (SIB-IMRT) to primary tumor (45.1 Gy and 40.04 Gy in 22 fractions) concurrently with S140 mg/m2, orally twice daily, 5 days/week) followed by surgery and four to six cycles of SOX at the same dosage with NACT arm. Surgery was scheduled to begin within 4-10 weeks of NACRT or NACT. The primary endpoint was surgical resection rate, second points were pathological response rate, postoperative complications, 3-year local control rate, disease-free survival, and overall survival. According to the plan design, 30 patients have to be enrolled for each arm. As for preliminary results, we investigated the effect of these two preoperative treatments on the pathologic parameters (ClinicalTrials.gov identifier, NCT02301481).

Results: From November 2013 to August 2015, 43 patients were randomly assigned to this trial: 22 in NACT arm (3 with stage II, 19 with stage III, AJCC 7th) and 21 in NACT arm (4 with stage II, 17 with stage III). Three patients did not undergo surgery because of tumor progression in each arm. R0 resection rate was 88.4% in NACT arm (19/22). Of 18 patients who underwent surgery after the first evaluation in NACT arm, 15 had R0 resection (71.4%, 15/21), with 1 receiving R1 and 1 receiving R2 resection. The other patient who was not a surgical candidate received additional chemoradiotherapy following NACT and finally received R0 resection. Pathologic response and complete pathologic response were achieved in 100% (19/19) and 21% (4/19) of patients in NACT arm, while 66.7% (12/18) and 11.1% (2/18) in NACT arm, respectively. More preoperative grade 1 to 3 thrombocytopenia occurred in NACT arm (38% vs 4.5%) and NACRT arm developed more dysphagia (45% vs 0%). There were no toxic deaths or postoperative deaths in both arms. Postoperative complications were similar in the two treatment groups (NACT vs NACRT, 4.4% vs 4.8%).

Conclusion: The design of preoperative concurrent SIB-IMRT with oral S-1 showed promising pathologic results with an acceptable toxicity profile, which encouraged future randomized phase III trials comparing NACT with NACT for resectable or unresectable gastric cancer.


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Randomized Trial of Hypofractionated Dose-Escalated Intensity Modulated Radiation Therapy Versus Conventionally Fractionated Intensity Modulated Radiation Therapy for Localized Prostate Cancer

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Purpose/Objective(s): Hypofractionated prostate radiotherapy shortens prostate cancer treatment duration and may increase biologically effective dose delivered to the prostate. We report cancer control and toxicity outcomes from a randomized trial testing the hypothesis that dose-escalated moderately hypofractionated radiation therapy improves prostate cancer control.

Materials/Methods: Two hundred six men with localized prostate cancer were randomized to conventionally fractionated intensity-modulated radiation therapy (CIMRT, 76.6 Gy in 1.8 Gy fractions) delivered over 8.4 weeks or to dose-escalated hypofractionated IMRT (HIMRT, 72 Gy in 2.4 Gy fractions) delivered over 6 weeks. Recurrence was defined as either PSA recurrence using the Phoenix definition of nadir plus 2 ng/mL, or initiation of salvage therapy. Late (> 90 days after completion of radiotherapy) genitourinary (GU) and gastrointestinal (GI) toxicity were graded using modified Radiation Therapy Oncology Group (RTOG) criteria.

Results: Most men had cT1 disease (72%), Gleason 6 (34%) or 7 (65%) disease, PSA <10 ng/mL (90%), and did not receive androgen deprivation therapy (76%). With a median follow up of 8.4 years, there were 31 recurrences. Men treated with HIMRT had fewer recurrences than men treated with CIMRT (P = 0.034). Eight-year recurrence was 10.7% (95% CI = 5.8-19.1%) with HIMRT and 15.4% (95% CI = 9.1-25.4%) with CIMRT. No one died from prostate cancer. There was no difference in overall survival between treatment groups (P = 0.37). Late grade 2 or 3 GU toxicity was similar between treatment groups (P = 0.83). There was a non-significant numeric increase in late grade 2 or 3 GI toxicity in men treated with HIMRT (8-year 5.0% vs. 12.6%; P = 0.08). There were no grade 4 toxicity events.

Conclusion: This moderate hypofractionation radiation treatment regimen of 72 Gy delivered in 2.4 Gy fractions shortens prostate cancer treatment duration and provides better prostate cancer control than 75.6 Gy delivered in 1.8 Gy fractions with acceptable toxicity.

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Long-Term Outcomes of a Phase 2 Trial of Moderate Hypofractionated Image Guided Intensity Modulated Radiation Therapy (IG-IMRT) for Localized Prostate Cancer

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University Health Network, Toronto, ON, Canada.

**Purpose/Objective(s):** To evaluate long-term biochemical control (bRFR) and radiation toxicity for men with localized prostate cancer treated with two moderately hypofractionated IG-IMRT regimens.

**Materials/Methods:** Eligible consenting men with T1c-T3a Nx M0 prostate cancer were enrolled in a phase II trial and received IG-IMRT to a risk-adapted volume that included prostate +/- seminal vesicles at 3 Gy per fraction, 5 days per week in sequential cohorts to a total dose of either 60 Gy or 66 Gy. Late gastrointestinal (GI) and genitourinary (GU) toxicity were recorded at each follow-up using the Radiation Therapy Oncology Group criteria and biochemical failure was scored using the PSA nadir + 2 criteria. Outcome estimates were calculated using the Kaplan-Meier method and log rank test. Early stopping rules terminated accrual to the 66 Gy cohort due to excessive Grade 3-4 late toxicity.

**Results:** Ninety-six men received 60 Gy and 28 received 66 Gy. Androgen deprivation therapy (3-36 months duration) was used in 10% of men in both cohorts. For each cohort, the median age was 71 years (60 Gy) and 70 years (66 Gy). Low or intermediate risk presentation was respectively 27% and 25% and 71% (66 Gy). Median follow-up was 128 months (66 Gy) and 108 months (60 Gy). The 5- and 8-year bRFR for 60 Gy and 66 Gy were respectively 83% and 76% vs 88.5% and 73.4% (P = 0.224). For each cohort, 5 (60 Gy) and 1 (66 Gy) subjects died from disease. Overall 5- and 8-year cumulative late Grade 1-4 GI toxicity for 60 Gy vs 66 Gy were, respectively, 21.2% and 21.2% vs 44.6% and 48.9% (P = 0.004). Cumulative late Grade 1-4 GU toxicities were, respectively, 23.8% and 32.8% vs 40.4% and 51.4% (P = 0.048). Cumulative 5- and 8-year late Grade 3-4 GI toxicity for 60 Gy and 66 Gy were respectively 1.1% and 1.1% vs 11.5% and 11.5% (P = 0.01). Cumulative 5- and 8-year late Grade 3-4 GU toxicity for 60 Gy and 66 Gy were respectively 0 and 1.5% vs 3.7% and 3.7% (P = 0.41). Late toxicities were self-limiting and at last follow-up in the 60 Gy cohort there were no Grade ≥ 3 late GI toxicities and one Grade 3 late GU toxicity. In the 66 Gy cohort there was one Grade 4 late GI toxicity and one Grade 4 late GU toxicity.

**Conclusion:** Moderate hypofractionation to 60 Gy was associated with modest late toxicity and provided excellent 5-year bRFR for our patients, although failures continued to be observed with subsequent follow-up. Dose escalation to 66 Gy was associated with significantly worse late GI and GU toxicity without an apparent improvement in bRFR.

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Concomitant Hypofractionated Intensity Modulated Radiation Therapy Boost For Localized High-Risk Prostate Cancer: Five-Year Results of a Prospective Trial

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**Purpose/Objective(s):** To report on the 5 year efficacy results of patients with localized high risk prostate cancer treated with a concomitant hypofractionated IMRT boost (simultaneous integrated boost) along with adjuvant androgen deprivation therapy (ADT).

**Materials/Methods:** From 2004-2010, a prospective phase I-II study was conducted in patients with any one or more of the following: T3 disease, PSA > 20 ng/mL, or Gleason score 8-10. A dose of 45 Gy in 25 fractions was delivered to the pelvic lymph nodes along with a concomitant IMRT boost of 22.5 Gy to the prostate, resulting in a total dose of 67.5 Gy in 25 fractions to the prostate over 5 weeks. Adjuvant ADT was to be delivered for 2-3 years. Biochemical failure was determined by the Phoenix definition. Univariate and multivariate analyses were performed to look for predictive factors. A post-treatment prostate biopsy was to be performed at 5 years to assess for pathologic local control.

**Results:** Two hundred thirty patients were treated and followed for the primary 5 year efficacy endpoint. Patients not lost to follow-up have a minimum follow-up of 5 years. Median age of patients was 72 years. Sixty-six percent had GS 8-10, 44% had PSA > 20 ng/mL, and 27% had T3 disease. The median duration of ADT was 30.4 months. Seventy-nine percent received at least 18 months of ADT. The median PSA nadir was 0.02 ng/mL. Ninety-two percent achieved a testosterone nadir of < 0.7 nmol/L. The 5 year probability of testosterone recovery (> 1.7 nmol/L) was 53.9%. The 5 year biochemical control rate was 83.7%. The 5 year overall survival was 93.7%. PSA nadir < 0.5 ng/mL independently predicted for higher biochemical control (HR 0.014; P < 0.0001), while a PSA nadir < 0.1 ng/mL independently predicted for longer overall survival (HR = 0.129; P = 0.0024). Starting ADT in an adjuvant fashion (vs neoadjuvant) independently predicted for higher biochemical control (HR = 0.419; P = 0.0116). ADT for ≤ 12 months independently predicted for worse overall survival compared to ADT for > 24 months (HR = 6.667; P = 0.014). Of the 45 patients who underwent a 5 year prostate biopsy, 5 (11.1%) had a positive result showing malignant cells with no radiation effect. The biochemical control and overall survival of patients who had a post-treatment biopsy were not different from those without a biopsy. The 5 year actuarial incidence of late grade ≥ 3 GI and GU toxicities were 1.9% and 7.2%, respectively.

**Conclusion:** A concomitant hypofractionated IMRT boost delivering 67.5 Gy in 25 fractions to the prostate over 5 weeks combined with elective pelvic nodal irradiation and adjuvant ADT resulted in favorable 5 year biochemical control and overall survival rates for patients with localized high risk prostate cancer. Lower PSA nadir predicted for higher biochemical control and longer overall survival. ADT duration of ≤ 12 months was associated with decreased overall survival. Pathologic local failure rate as assessed by 5 year post-treatment biopsy was low.


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Five-Year Outcomes From a Multicenter Trial of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer

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**Purpose/Objective(s):** Single-institution studies suggest stereotactic body radiotherapy (SBRT) is a cost-effective alternative to IMRT as primary therapy for prostate cancer. We hypothesized that dose-escalated SBRT could be safely administered across multiple institutions, with grade 3+ toxicities not exceeding 10%. With median follow up greater than 5 years, we report toxicity, survival, and relapse-free survival (RFS) outcomes.

**Materials/Methods:** After completing rigorous credentialing requirements, 21 community, regional, and academic hospitals enrolled 309 evaluable patients with biopsy-proven adenocarcinoma of the prostate, confirmed by central pathologic review: 172 low-risk (CS T1-T2a, Gleason 6, PSA < 10 ng/mL) and 137 intermediate-risk (CS T1c-T2b with either Gleason 7 and PSA < 10 ng/mL, or Gleason 6 and PSA between 10 and 20 ng/mL). All patients were treated with a non-isocentric robotic SBRT