Methods and Materials: From April 1995 through March 2003, 1,093 consecutive patients underwent brachytherapy for clinical T1b–T3a (2002 AJCC) prostate cancer. The median follow up was 5.6 years. All patients were implanted at least 3 years prior to analysis. Evaluated body mass index (BMI) subgroups were <25 (n = 258), 25.0 to 29.9 (n = 547), 3.0 to 3.49 (n = 214) and >35 (n = 74) kg/m², respectively. Four hundred thirty (39.9%) and 589 (53.9%) of the patients received androgen deprivation therapy or supplemental external beam radiation therapy, respectively. Multiple clinical, treatment and dosimetric parameters were evaluated as predictors of CSS, bPFS and OS.

Results: The 11-year CSS, bPFS and OS for the entire cohort were 97.5%, 95.6%, and 77.6%, respectively. BMI did not impact CSS or bPFS for any of the BMI cohorts. However, OS was statistically lower in patients with a BMI >35 (p = 0.014). A Cox linear regression analysis demonstrated that Gleason score was the best predictor of CSS while percent-positive biopsies, risk group, V100 and hypertension predicted for bPFS. Patient age and tobacco use were the strongest predictors of OS. One hundred twenty-eight patients have died with 108 (84.4%) of the deaths the result of cardiovascular/pulmonary disease (73) and second malignancies (35). To date, 12 patients have died of metastatic prostate cancer.

Conclusions: Following brachytherapy, obesity did not impact CSS, bPFS or OS. Cardiovascular or pulmonary disease and second malignancies substantially outweighed prostate cancer as competing causes of death.

PO-3
Evaluation of seed placement accuracy with a novel brachytherapy robot
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Purpose: One of the primary benefits of a robot designed for brachytherapy implantation is accuracy. We sought to create a device that could deposit seeds with sub-millimeter displacement error. To achieve this goal, certain necessary needle parameters needed to be optimized. To date, we have evaluated parameters including insertion speed, needle rotation techniques and force requirements. We have designed a robot capable of inserting a needle to the desired position using a modified needle rotation technique that minimizes tissue damage while still maintaining a reduction in friction. This reduction in friction leads to better seed placement because of reduced compression of the prostate. Now, we look to validate our optimizations by measuring the seed deposition accuracy of the device in a gel phantom.

Methods and Materials: The brachytherapy robot is a 6 degree of freedom manipulator designed and optimized for brachytherapy procedures. Using the robot, 13 seeds were implanted into a 300 bloom strength gel phantom formulated to have a similar Young’s Modulus to that of human prostate tissue. The seeds were implanted with reference to a point of origin. Seed position relative to this point was measured using an orthogonal film technique.

Results: Seed placement accuracy was measured along the x, y, and z directions. The average error in seed positioning in these dimensions was 0.78 ± 0.51 mm, 0.27 ± 0.34 mm, and 0.11 ± 0.20 mm, respectively. The average total displacement error per seed is 0.83 ± 0.65 mm.

Conclusions: Sub-millimeter accuracy can be achieved in phantom with this brachytherapy robot. The results of this experiment are a positive reinforcement that the device can reach our goal in tissue. Furthermore, the seed rotation capabilities of the device will be used in conjunction with the new directional sources designed within our group, leading to an advancement in prostate brachytherapy. Future work with animal studies is an important step in the robot’s progression towards clinical use.

PO-4
The time gap between Pd-103 prostate brachytherapy and supplemental beam radiation does not impact on rectal morbidity or likelihood of cure
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Purpose: To determine whether treatment gap between supplemental beam radiation and brachytherapy implant affects rectal morbidity and likelihood of cure in the treatment of intermediate-risk prostate cancer.

Methods and Materials: Five hundred sixty-eight patients with AJCC clinical stage T1c–T2a prostate cancer, Gleason score 7–9 and/or PSA 10–20 ng/mL, were randomized to implantation with Pd-103 (90 versus 115 Gy) with 44 Gy versus 20 Gy pre-implant supplemental beam radiation, respectively. Treatment-related morbidity was monitored by mailed questionnaires, using a modified Radiation Therapy Oncology Group (RTOG) rectal morbidity criteria at 1, 3, 6, 12, 18, and 24 months. Patients who reported Grade 1 or worse rectal morbidity were interviewed by telephone to clarify details regarding their rectal bleeding.

Results: Persistent rectal bleeding occurred in 36 of the 548 evaluable patients (7%). The mean gap among rectal bleeders was 3.8 days and among non-bleeders was 4.8 days (p = 0.236). Higher R100 (RR-1.40; p = 0.047) and external beam dose of 44 Gy (RR-2.22; p = 0.047) were significant predictors of rectal bleeding on univariate and multivariate analysis. Log-rank analysis did not demonstrate any improvement in biochemical failure free survival (BFFS) with shorter gap interval. On univariate analysis, Gleason score >7, PSA >10, D50 <100 Gy, and treatment gap were all predictive of biochemical failure. On multivariate analysis, only Gleason score (HR-3.60, p < 0.001), PSA (HR-2.17, p = 0.002), and D50 (HR-3.25, p < 0.001) remained significant predictors of BFFS.

Conclusions: Shorter gap intervals between supplemental beam radiation and brachytherapy implant are safe. While shorter gap intervals do not improve BFSS, they do allow for treatment completion in a more timely fashion.

PO-5
The role of tropism chloride in brachytherapy-related urinary morbidity
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Purpose: Following prostate brachytherapy, severe urinary frequency, urgency and nocturia occur in a substantial minority of patients. In the general population, tropism chloride (an antimuscarinic agent) represents effective medical management for an overactive bladder in most patients. In this study, we evaluated the impact of tropism in prostate brachytherapy patients with overactive bladder symptomatology.

Methods and Materials: Seventy-two patients implanted between January 1999 and January 2006 with Pd-103 or I-125 were identified who received tropism as “first-line” treatment for detrusor overactivity. The mean interval from implant to initiation of tropism was 2.5 years. Prior to initiation of tropism, a post-void residual urine assessment (PVR) and IPSS evaluation was obtained for all patients. Response to medical therapy was evaluated by IPSS (overall and individual questions) resolution and PVR trends. Overall IPSS resolution was defined as a return to within 2 points of baseline and individual IPSS question resolution was defined by a decrease in each individual question of 2 or more points. Multiple clinical, treatment and dosimetric parameters were evaluated as predictors for response.

Results: The mean patient age was 65.4 years with a pre-brachytherapy prostate volume of 31.2 cm³ and a mean pre-implant IPSS of 6.6. At the initiation of tropism the mean IPSS was 13 with a mean PVR of 10.4 cc. Of the 72 patients, overall IPSS normalization was documented in 55 (76.4%) patients. Twelve months following tropism initiation, the IPSS on average had decreased to a value 5 points less than baseline. In terms of individual IPSS questions, tropism related responses were limited to frequency, urgency and nocturia. The remaining 4 IPSS questions
(emptying, interruption, strength of stream and straining) were not influenced by tropsium. Following the initiation of medical therapy, postvoid residual urine was 52 cc at 2 months and 26 cc at 12 months. On average the mean time of tropsium usage was 7 months. Twenty-one patients discontinued tropsium secondary to no response or pharmacologic induced side effects.

Conclusions: Approximately three-quarters of patients with brachytherapy-related urinary urgency, frequency and nocturia responded favorably to tropsium.

PO-6
The relationship between isotope and learning curve in patients undergoing permanent prostate brachytherapy: Analysis of the Pro-Qura database
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Purpose: To analyze the Pro-Qura database for evidence of a postimplant dosimetric learning curve stratified by isotope.

Methods and Materials: In the Pro-Qura database, 2,933 post-plans were analyzed from 57 institutions for evidence of an isotope-based dosimetric learning curve. The mean and median time between implant and postimplant CT scan was 30 days. I-125 was used 2,198 cases and Pd-103 in 725. The mean I-125 seed activity was 0.32 mCi and 0.25 mCi for monotherapy and boost while for Pd-103 the mean seed activity was 1.59 mCi and 1.25 mCi, respectively. Pre-implant prostate volume was 35.3 cm$^3$ and 32.9 cm$^3$ in the I-125 and Pd-103 cohorts, respectively. Postimplant dosimetry was performed in a standardized fashion by overlaying the pre-implant ultrasound and the postimplant CT scan.

Criteria for implant adequacy included a D$_{90}$ >90% and a V$_{100}$ >80% for both isotopes. An adequate V$_{100}$ was defined as <60% for I-125 and <75% for Pd-103. A D$_{90}$ >140% was deemed “too hot.”

Results: When stratified by patient sequence number for each institution, the mean V$_{100}$ increased from 88.1% to 90.5% for I-125 and remained unchanged for Pd-103 (85.0% to 84.7%) for implant patient numbers 10–80. D$_{90}$ increased from 104% to 105% for I-125 and from 93.6% to 94.8% for Pd-103. Overall 16% of I-125 and 30% of Pd-103 implants were deemed “too cool” while 23% of I-125 implants and 4% of Pd-103 implants were deemed “too hot.”

Conclusions: Within the confines of this study, no clinically meaningful dosimetric improvements for either isotope were noted with increasing experience. Overall 16% of I-125 and 30% of Pd-103 implants were deemed “too cool.”

PO-7
Divide and conquer: Postimplant dosimetry using fractional seeds
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Purpose: Seed identification is of central importance to the evaluation of brachytherapy implants. Various CT and film-based seed localization systems are available, but to our knowledge, none is robust enough to perform this task without user intervention. (Seed localization via scout images, as suggested for head-and-neck treatments, has limited usefulness for prostate implants.) To obtain the dose distribution in the implant (and at the same time circumvent this shortcoming), we propose the following ad hoc method: every signature of every seed is digitized as a seed fragment (fractional seed) on every image of the 3D study, and is assigned air kerma strength ($S_k$) equal to the ratio of the total implanted $S_k$ to the total number of seed fragments. In this work we defend the idea that the dose distribution thus obtained serves as a useful substitute to the actual dosimetry.

Methods and Materials: A 3-film reconstruction technique is used to obtain accurate seed coordinates. Because the film lacks volumetric information an application (NavilSeed) was developed to register the film reconstruction result to CT images. Specifically, a graphical user interface is provided to fuse the coordinate systems of the films and CT images. After registering the two coordinate systems, the user can navigate the seeds at each CT slice in a full 3D browser. This coupled information can assist the user to identify the locations of seeds on each CT slice. Such a scheme provides accurate dosimetry and will be used here to benchmark the dosimetry of fractional seeds. CT-based dosimetry was performed using VareiSeed™ version 7.1 (Varian Medical Systems, Inc., Palo Alto, CA). Dosimetric indices (prostate V$_{100}$, D$_{90}$, urethra D$_{90}$, and rectum D$_{20}$, D$_{5}$) as obtained with the two techniques are compared.

Results: A sample of representative patients was used for dosimetric comparisons. In most cases we find good agreement (1–3%) between the two methods. In some cases, when seeds are very close to a critical structure, we find that seed position may play a slightly more dominant role exhibited in the maximum organ dose. But even in these extreme cases, the discrepancy is within 10%.

Conclusions: The fractional seed method is a robust and reliable tool for postimplant dosimetry and is amenable to operator-independent implementation. It circumvents the need for an algorithm that “decides” which seed fragments correspond to an actual seed, and thus avoids seed identification inaccuracies. As well, it paves the way for fully automated intraoperative CT-based postimplant evaluations.

PO-8
Preliminary review of radical prostatectomy versus brachytherapy for prostate cancer treatment
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Purpose: This is a retrospective comparison of patients treated with radical prostatectomy or brachytherapy at Gunderson Lutheran between January 1996 and May 2003.

Methods and Materials: We divided the patients into 3 risk categories: low (Gleason 6, PSA <10 and <50% positive biopsies), intermediate (only one of any biopsy cores with Gleason 7, or PSA 11–19 or 50% of the biopsies positive) and high (all remaining patients). In total, there were 313 low (prostatectomy = 131, brachytherapy = 182), 220 intermediate (prostatectomy = 85, brachytherapy = 135), and 176 high (prostatectomy = 71, brachytherapy = 105), risk patients. The brachytherapy patients who were intermediate or high risk received external beam radiation (45 Gy) plus brachytherapy. Nearly all our brachytherapy implants were Pd-103. We compared biochemical event free survival at 7 years defining treatment failure for prostatectomy as a PSA >0.2 and for brachytherapy as a PSA >1.

Results: For low risk patients there was no statistical difference between biochemical event free survival for prostatectomy, 79.2%, and brachytherapy, 88.0% (p = 0.432). For intermediate risk patients, there was no statistically significant difference (p = 0.050) between the two modalities (prostatectomy 68.2% vs. brachytherapy 87.9%), though a trend favoring brachytherapy may be evolving. For the high risk patients, the brachytherapy group showed a statistically significant increase in biochemical event free survival, 77.8% vs. 47.6% for prostatectomy (p = 0.014).

Conclusions: From these results, we conclude prostatectomy and seed implantation are equally efficacious for our low risk patients. A trend favoring brachytherapy for intermediate risk patients may be evolving, but this has not reached statistical significance. The combination of external beam radiation therapy followed by seed implantation appears to result in superior biochemical event free survival for high risk patients when compared to radical prostatectomy.