6.1 Dose Specifications (4/20/16)

6.1.1 Phase 1: Sequential Boost Technique

- **Arm 1**: Treat prostate and seminal vesicles
  Acceptable Treatment Modalities: 3D-CRT or IMRT

  Prescribed Dose (See Table 1.1)
  45 Gy Rx to cover at least 98% of PTV_4500
  - Minimum dose within PTV_4500 – 95% of prescribed dose and for a volume that is 0.03 cc
  - Maximum dose within the PTV_4500 – 107% of prescribed dose and for a volume that is 0.03 cc

<table>
<thead>
<tr>
<th>Table 1.1: 3D-CRT and IMRT Dose Objectives for Phase 1, Arm 1 – Prostate and Seminal Vesicles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage</td>
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<tr>
<td>Minimum Dose</td>
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<tr>
<td>Maximum Dose</td>
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<tr>
<td>Homogeneity</td>
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</tbody>
</table>

**Dmax in Patient**: In PTV_4500

*Note: Dosimetric and/or volumetric parameters falling outside the Per Protocol and Variation Acceptable specifications are classified as Deviation Unacceptable. % Dose are normalized to Rx dose = 45 Gy. Dmin and Dmax are to 0.03 cc volume.*

- **Arm 2**: Treat whole pelvis including prostate and seminal vesicles
  Acceptable Treatment Modalities: 3D-CRT or IMRT

  Prescription Dose (See Table 1.2)
  45 Gy Rx to cover at least 98% of PTV

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3.0 PATIENT SELECTION
NOTE: PER NCI GUIDELINES, EXCEPTIONS TO ELIGIBILITY ARE NOT PERMITTED

3.1 Conditions for Patient Eligibility (4/27/15)

For questions concerning eligibility, please contact the study data manager.

3.1.1 Pathologically (histologically or cytologically) proven diagnosis of prostatic adenocarcinoma within 180 days of registration at moderate to high risk for recurrence as determined by one of the following combinations:
- Gleason score 7-10 + T1c-T2b (palpation) + PSA < 50 ng/ml (includes intermediate and high risk patients);
- Gleason score 6 + T2c-T4 (palpation) + PSA < 50 ng/ml

**OR:**
- Gleason score 6 + ≥ 50% (positive) biopsies + PSA < 50 ng/ml;
- Gleason score 6 + T1c-T2b (palpation) + PSA > 20 ng/ml.

Patients previously diagnosed with low risk prostate cancer undergoing active surveillance who are re-biopsied and found to have unfavorable intermediate risk disease or favorable high risk disease according to the protocol criteria are eligible for enrollment within 180 days of the repeat biopsy procedure.

3.1.2 History/physical examination (to include at a minimum digital rectal examination of the prostate and examination of the skeletal system and abdomen) within 90 days prior to registration.

3.1.3 Clinically negative lymph nodes as established by imaging (pelvic ± abdominal CT or MR), (but not by nodal sampling, or dissection) within 90 days prior to registration.
- Patients with lymph nodes equivocal or questionable by imaging are eligible if the nodes are ≤ 1.5 cm.

3.1.4 No evidence of bone metastases (M0) on bone scan within 120 days prior to registration (Na F PET/CT is an acceptable substitute).
- Equivocal bone scan findings are allowed if plain films (or CT or MRI) are negative for metastasis.

3.1.5 Baseline serum PSA value performed with an FDA-approved assay (e.g., Abbott, Hybritech) within 120 days prior to registration.
- Study entry PSA should not be obtained during the following time frames: (1) 10-day period following prostate biopsy; (2) following initiation of hormonal therapy; (3) within 30 days after discontinuation of finasteride; (4) within 90 days after discontinuation of dutasteride.

3.1.6 Zubrod Performance Status 0-1 (unless otherwise specified);

3.1.7 Age ≥ 18;

3.1.8 CBC/differential obtained within 60 days prior to registration on study, with adequate bone marrow function defined as follows:
- Absolute neutrophil count (ANC) ≥ 1,500 cells/mm³;
- Platelets ≥ 100,000 cells/mm³;
- Hemoglobin ≥ 8.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8.0 g/dl is acceptable);

3.1.9 Patient must be able to provide study specific informed consent prior to study entry.

3.2 Conditions for Patient Ineligibility (2/26/14)

3.2.1 Prior invasive (except non-melanoma skin cancer) malignancy unless disease-free for a minimum of 3 years (1095 days) not in the pelvis. (For example, carcinoma in situ of the oral cavity is permissible; however, patients with prior history of bladder cancer are not allowed).
- Prior hematological (e.g., leukemia, lymphoma, myeloma) malignancy not allowed.

3.2.2 Previous radical surgery (prostatectomy) or cryosurgery for prostate cancer

3.2.3 Previous pelvic irradiation, prostate brachytherapy, or bilateral orchietomy

3.2.4 Previous hormonal therapy, such as LHRH agonists (e.g., leuprolide, goserelin, buserelin, triptorelin) or LHRH antagonist (e.g. degarelix), anti-androgens (e.g., flutamide, bicalutamide, cyproterone acetate), estrogens (e.g., DES), or surgical castration (orchietomy)
- Prior pharmacologic androgen ablation for prostate cancer is allowed only if the onset of androgen ablation (both LHRH agonist and oral anti-androgen) is ≤ 45 days prior to the date of registration. Please refer to Section 7.1.1 for timing of oral anti-androgen administration with the LHRH agonist.

3.2.5 Use of finasteride within 30 days prior to registration

3.2.6 Use of dutasteride or dutasteride/tamsulosin (Jalyn) within 90 days prior to registration

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3.2.7 Previous or concurrent cytotoxic chemotherapy for prostate cancer; note that prior chemotherapy for a different cancer is allowable. See Section 3.2.1.

3.2.8 Prior radiotherapy, including brachytherapy, to the region of the study cancer that would result in overlap of radiation therapy fields

3.2.9 Severe, active co-morbidity, defined as follows:

- Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
- Transmural myocardial infarction within the last 6 months
- Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
- Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration
- Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects or severe liver dysfunction
- Acquired immune deficiency syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive. Protocol-specific requirements may also exclude immuno-compromised patients.

3.2.10 Patients who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.

3.2.11 Prior allergic reaction to the hormones involved in this protocol

3.2.12 Patients status post a negative lymph node dissection are not eligible