

# Hypofractionation Treatment of Favorable Intermediate-risk Prostate Cancer

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## Introduction

This research-based project will demonstrate the efficacy of a moderate hypofractionated regimen for the treatment of favorable intermediate-risk prostate cancer. Prostate cancer is a major cause of disease and mortality among men. Research indicates that each year, 1.6 million men are diagnosed with it and 366,000 die from it. Diagnosis is based on rectal examination, serum prostate specific antigen (PSA) measurement, and when essential, transrectal prostate needle biopsy followed by a Gleason score obtained from it. When treating prostate cancer, identifying a Gleason score is the deciding factor in choosing from a wide spectrum of treatment options ranging from supervision to multimodal treatment. Upon completion of essential tests, the primary tumor is assigned a stage based on the American Joint Committee on Cancer's (AJCC) 8<sup>th</sup> edition Tumor Node Metastasis (TNM) staging system for prostate cancer and the patient is placed in a risk group. If radiation therapy treatment is required, the patient will undergo a process consisting of a treatment simulation followed by treatment planning. The preferred External Beam Radiation Therapy (EBRT) regimen is moderate hypofractionation. This prospect focuses on a case study of a 54-year-old gentleman who successfully underwent pelvic radiation therapy using hypofractionation doses for the treatment of prostate cancer.

## Prostate Cancer

- Is unregulated, uncontrolled replication of cells in the prostate (Long, Rollins, & Smith, 2019)
- Is the most diagnosed cancer in men with approximately 1.6 million incident cases in 2015 (Pernar, Ebot, Wilson, & Mucci, 2018)
- Is the second most common cause of cancer death among men in the United States (Pernar et al., 2018)
- Is rare among men younger than forty years of age, with incidence rates increasing after age fifty-five (Pernar et al., 2018)
- Is responsible for the diagnosis of 191,930 men in the United States in 2020 (Siegel, Miller, & Jemal, 2020)
- Is diagnosed on average at age sixty-six years (Pernar et al., 2018)

## Risk Factors

- Men between ages of 75 to 84 years have the highest rate of mortality (Vane, 2019)
- Men with diagnosed paternal relatives are at two-fold to three-fold higher risk of being positive (Pernar et al., 2018)
- Men with paternal relatives who died of prostate cancer have two-fold higher risk of death compared with men without a family history (Pernar et al., 2018)
- Modifiable risk factors
  - Alcohol use (Vane, 2019)
  - Obesity (Vane, 2019)
  - Cigarette smoking (Vane, 2019)
  - High-fat diet (Vane, 2019)

## Diagnosing Prostate Cancer

- Physical examination by physician
- Digital rectal examination (DRE)
- Serum prostate specific antigen (PSA) measurement
  - Threshold should be less than 4.0 ng/dl (Vane, 2019)
  - Velocity increases correlate with risk, aggressiveness, and can indicate presence of prostate cancer (Catalona, 2018)
- Transrectal ultrasound-guided prostate needle biopsy
  - Provides information about tumor pathology (Öztürk & Yıkılmaz, 2018)
- Gleason score
  - First and second most common glandular patterns identified (Öztürk & Yıkılmaz, 2018)
  - Important in terms of disease course and treatment planning (Öztürk & Yıkılmaz, 2018)
  - Pathological scores range from 2 to 10

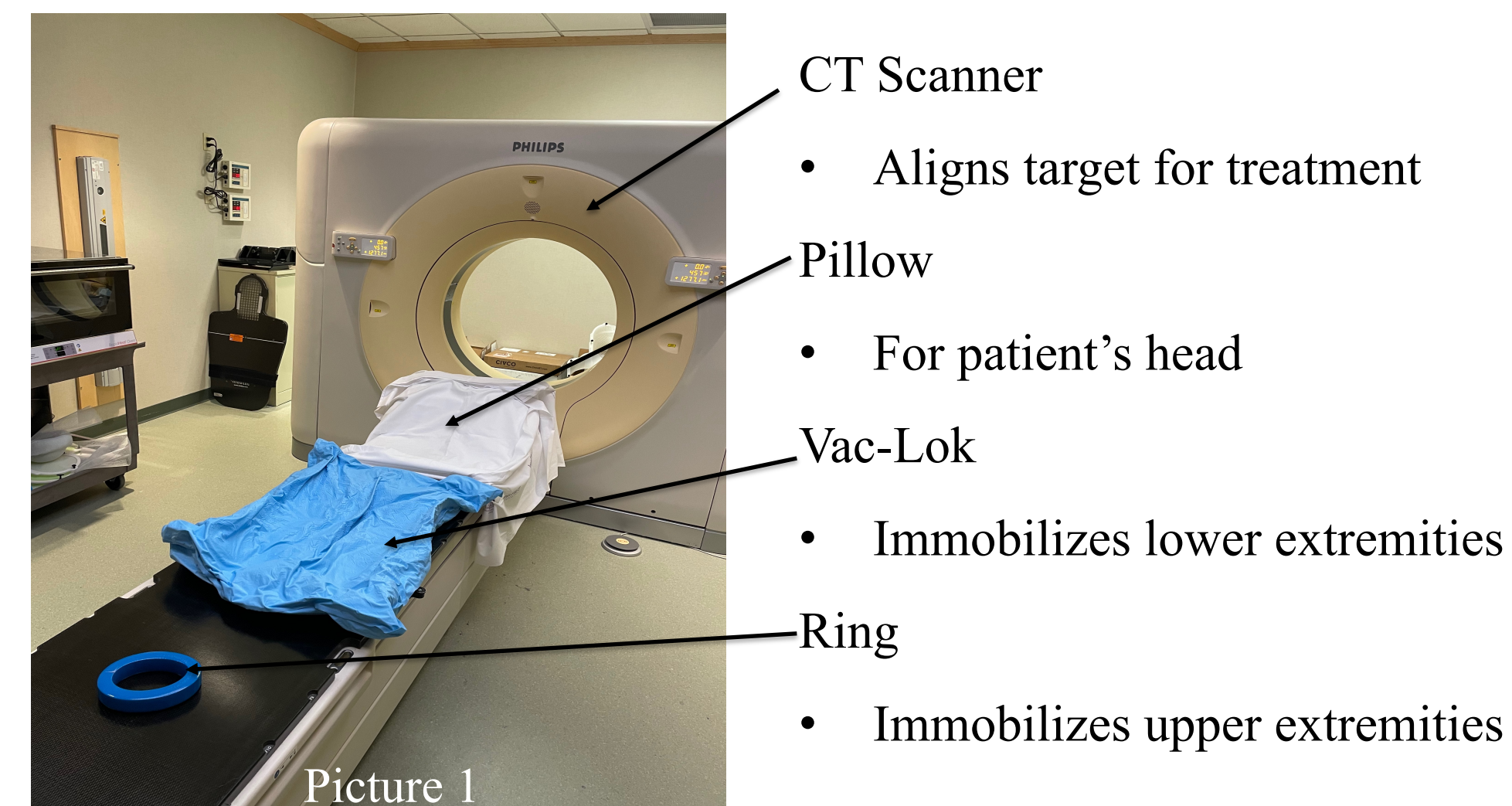
## Patient Demographics & Medical History

- 54-year-old, male patient
  - Presented with voiding complaints including frequency of urination and awakening once per night to void
  - Family history of prostate cancer: brother diagnosed at age 61 and treated with radiation
  - PSA levels were monitored
    - **03/12/17** 2.09 ng/ml PSA
    - **04/14/18** 2.2 ng/ml PSA
    - **04/14/19** 2.93 ng/ml PSA
- (Delta Medix, 2020)

## Patient Treatment Planning

- **06/06/20** 4.57 ng/ml PSA
    - Abnormal 1.64 ng/ml PSA Velocity increase in 1 year
  - **07/16/20** Transrectal ultrasound-guided needle biopsy of prostate
    - Gleason score 3+4 = 7, on right lateral base, right lateral mid, right medial mid, and right medial apex involving 40% to 60% of invasive adenocarcinoma on prostate
      - Perineural invasion present in some biopsy cores
    - Gleason score 3+3 = 6, on right lateral apex involving 15% of invasive adenocarcinoma on prostate; no perineural invasion
      - Negative remaining 7/12 biopsy cores
  - Patient was diagnosed with favorable intermediate-risk prostate cancer
    - Diagnosed with stage IIB, T1c, N0, M0, Grade group 2, Gleason score 3+4 = 7, invasive adenocarcinoma on right side of prostate (refer to figures 1 and 2)
  - **08/17/20** Bone scan and CT of abdomen and pelvis
    - Negative for tumor metastasis
  - **11/30/20** Hypofractionation treatment began
    - Total dose prescribed of 7,000 cGy delivered in 28 fractions (250 cGy per fraction)
  - **01/12/21** Hypofractionation treatment ended
    - Patient reported episodes of mild loose stool at times for 2 weeks, loss of taste, and decrease in appetite
  - **01/23/21** 0.46 ng/ml PSA
    - PSA level below threshold
  - **02/11/21** Treatment follow-up
    - Patient reported nocturia once per night, hot flashes (from androgen deprivation therapy); everything else was negative
  - **07/25/21** 0.49 ng/ml PSA
    - PSA level below threshold
  - **08/2021** Treatment follow-up
    - Patient reported nocturia; hot flashes have subsided
- (Delta Medix, 2020)

## Treatment Simulation



- Aligns target for treatment
- For patient's head
- Immobilizes lower extremities
- Immobilizes upper extremities
- Treatment setup is simulated by positioning the patient on the flat couch going into the unit headfirst, holding onto ring
- A Vac-Lok immobilization device that minimizes patient movement is made simultaneously
- The patient is aligned to the lasers in the room and marked on the skin with tattoos
- A CT scan will be done to guide the linear accelerator to target the lesions accurately and spare critical organs as much as possible during treatment

## Prostate Cancer Staging

### The TNM System

<b>Tumor</b>	T1: Clinically inapparent tumor that is not palpable T2: Palpable tumor confined within prostate T3: Extraprostatic tumor that does not invade/unfixed T4: Tumor is fixed/invades structures other than seminal vesicles
<b>Node</b>	NX: Regional lymph nodes cannot be assessed N0: No positive regional nodes N1: Metastases in regional node(s)
<b>Metastasis</b>	M0: No distant metastasis M1: Distant metastasis

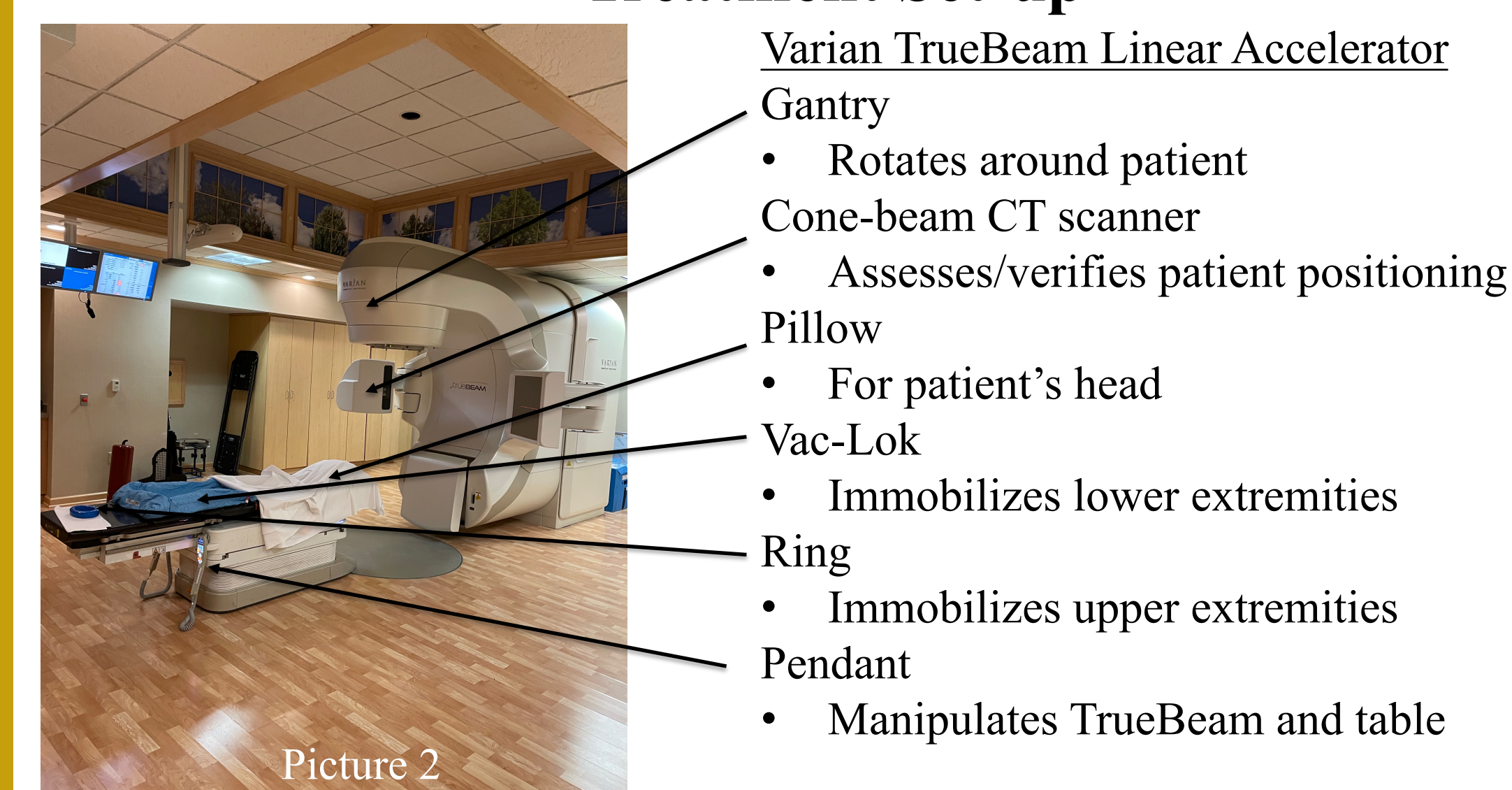
Figure 1

### Risk Stratification Workup

Risk Group	Grade Group	Gleason Score	PSA
Low/Very Low	1	≤ 6	< 10
Intermediate (Favorable/Unfavorable)	2	7 (3+4)	10 – 20
	3	7 (4+3)	
High/Very High	4	8	> 20
	5	9 – 10	

Figure 2

## Treatment Set-up

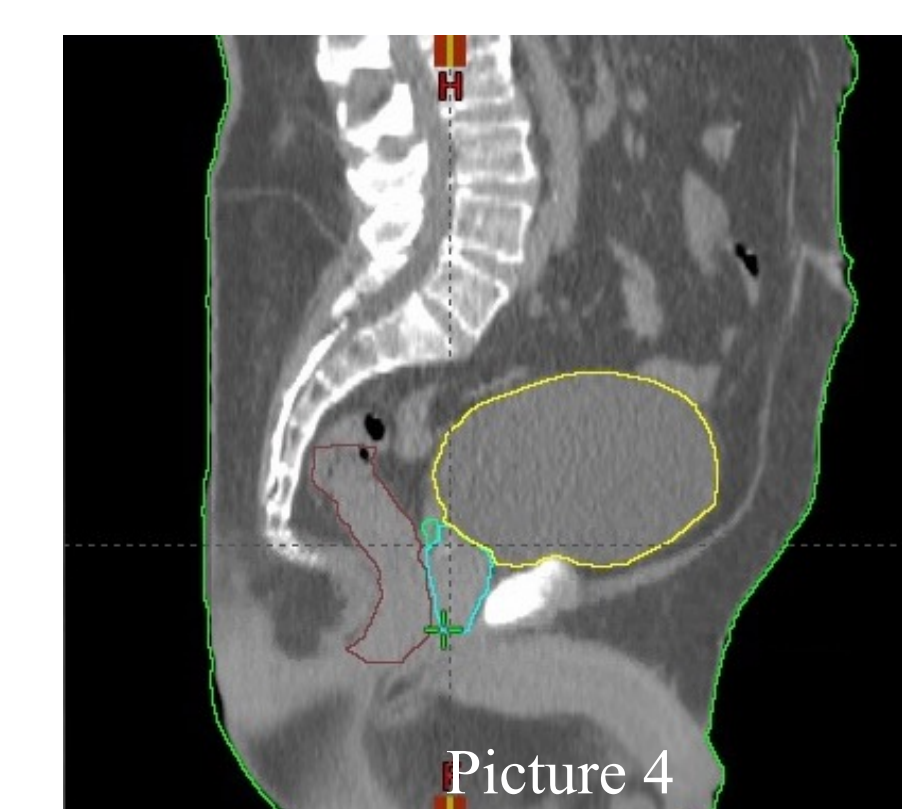


### Varian TrueBeam Linear Accelerator

- Rotates around patient
- Assesses/verifies patient positioning
- For patient's head
- Immobilizes lower extremities
- Immobilizes upper extremities
- Manipulates TrueBeam and table



- Bladder
- Prostate Gland
- Seminal Vesicles
- Rectum
- Femoral Head + Greater Trochanter
- Femoral Head + Greater Trochanter



- Bladder
- Prostate Gland
- Seminal Vesicles
- Rectum

## Clinical/Pathologic Features: Intermediate Risk Group

- Refer to figure 2
  - No very high/high-risk group features
  - Grade group 2 or 3
  - Gleason score of 7 (3+4) or (4+3)
  - PSA 10 – 20 ng/mL
- (Schaeffer et al., 2021)

## Intermediate Risk Group

- Does not require treatment of pelvic lymph nodes (eviCore healthcare, 2021)
- Hypofractionation radiation-therapy strongly recommended (eviCore healthcare, 2021)
- Two subcategories
  - Favorable intermediate
  - Unfavorable intermediate

### Favorable intermediate

- Grade group 1 or 2
  - <50% biopsy cores positive (eg, <6 of 12 cores)
    - Prophylactic lymph node radiation and ADT or antiandrogen therapy is not used routinely
      - Reasonable if additional risk assessments suggest aggressive tumor behavior
  - Preferred Hypofractionated dose regimens that have shown acceptable efficacy and toxicity
    - 3 Gray x 20 fractions
    - 2.7 Gray x 26 fractions
    - 2.5 Gray x 28 fractions
- (Schaeffer et al., 2021)

## Hypofractionation Radiation Therapy Facts

- Fraction size between 240 centigrays and 340 centigrays (eviCore healthcare, 2021)
- Regimens of 6000 centigrays in 20 radiation treatment fractions and 7000 centigrays in 28 radiation treatment fractions suggested (eviCore healthcare, 2021)
- Increases tumor cell killing without causing a corresponding increase in damage to surrounding healthy tissues (Campos et al., 2021)
- Reduces overall treatment time, number of hospital trips, and use of linear accelerator, thus benefiting patients and treatment centers (Campos et al., 2021)
- Advantageous for radiation therapy treatment centers with limited resources, long waiting lists, and/or a geographically dispersed population in which many patients live far from the center (Campos et al., 2021)
- No overall difference in severe gastrointestinal and genitourinary toxicity between non-hypofractionated and hypofractionated regimens (Sujenthiran et al., 2020)

## Conclusion

This research-based project was done to demonstrate the efficacy of a moderate hypofractionated regimen for the treatment of favorable intermediate-risk prostate cancer. This 54-year-old male patient was prescribed a total dose of 7,000 centigrays to be delivered in 28 fractions (250 centigrays per fraction). He received a total dose of 7,000 centigrays as prescribed over 43 elapsed days. After completion of the treatment, he reported episodes of mild loose stool at times for two weeks, loss of taste, and decrease in appetite. One month later he reported nocturia once per night and hot flashes. Six months later he reported nocturia but no more hot flashes. His PSA was 4.57 ng/ml on 06/06/20 prior to the start of treatment. Upon treatment completion, his PSA was measured to be 0.46 ng/ml on 01/23/21 and 0.49 ng/ml on 07/25/21. The PSA level decreases demonstrate the efficacy of the hypofractionated regimen for the treatment of favorable intermediate-risk prostate cancer. This regimen shows no overall difference in severe gastrointestinal and genitourinary toxicity and reduces the overall treatment time, the number of hospital trips, and use of the linear accelerator, thus benefiting patients as well as treatment centers.