

## Early-stage prostate cancer treatment alternatives

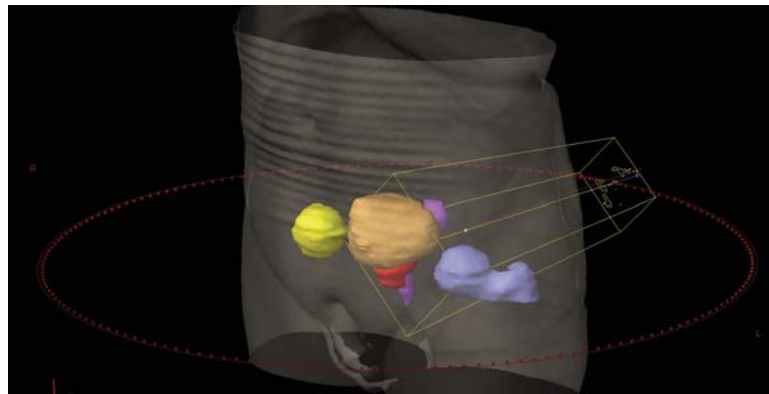
The American Cancer Society estimates that 186,320 new **prostate cancer** cases occurred in the United States during 2008,<sup>1</sup> making it the most frequently diagnosed cancer in men. Prostate cancer is one of the leading causes of cancer death in men, but mortality is only 15% of incidence due to slow tumor growth and an older population, with 28,660 deaths in 2008.<sup>1</sup>

Over the past 20 years, the annual age-adjusted incidence of prostate cancer has increased, likely due to prostate-specific antigen (PSA) screening<sup>2</sup> and increased use of transurethral prostate resection for the relief of urinary obstruction.<sup>3</sup> Risk factors include age and family history with incidence significantly higher for African Americans.<sup>1</sup>

Early detection is recommended with a digital rectal exam and a PSA test in all men over the age of 50.<sup>1</sup> Opinions differ regarding the importance of absolute PSA, PSA velocity, and the optimal frequency of repeating the PSA. About 38% of men will die with unsuspected prostate cancer, which highlights the chronicity of the cancer.<sup>4</sup>

Treatment options vary depending upon the patient's age, cancer stage, and confounding medical conditions. These include surgery, brachytherapy (BT), external beam radiation, and stereotactic body radiation therapy (SBRT). Varian Medical Systems provides solutions for these three radiotherapy options, including RapidArc radiotherapy,<sup>5</sup> backed by years of clinical research at centers using these options.<sup>5, 6, 11, 12, 13, 14, 15, 16, 18</sup> Another option is "watchful waiting," or careful observation, which may be appropriate for older men with small, non-aggressive tumors, low Gleason scores and low PSA levels.<sup>6</sup>

Given the multiple therapeutic options, patients have a choice of therapy which requires informed consent with an understanding of the PSA control, toxicity, and cost. Higher radiation doses yield better tumor control.<sup>6</sup> Intensity-modulated radiation therapy (IMRT) and brachytherapy reduce normal tissue toxicity.<sup>6</sup> Acute toxicities and quality-of-life related issues from surgery—such as pain, blood loss, infection, hospital stay, and surgical recovery—are not included in the table on the back. Also not included are the important toxicities of erectile dysfunction<sup>7</sup> and penile shortening.<sup>8</sup>



RapidArc™ radiotherapy technology for prostate cancer: sub-minute treatment with higher conformality

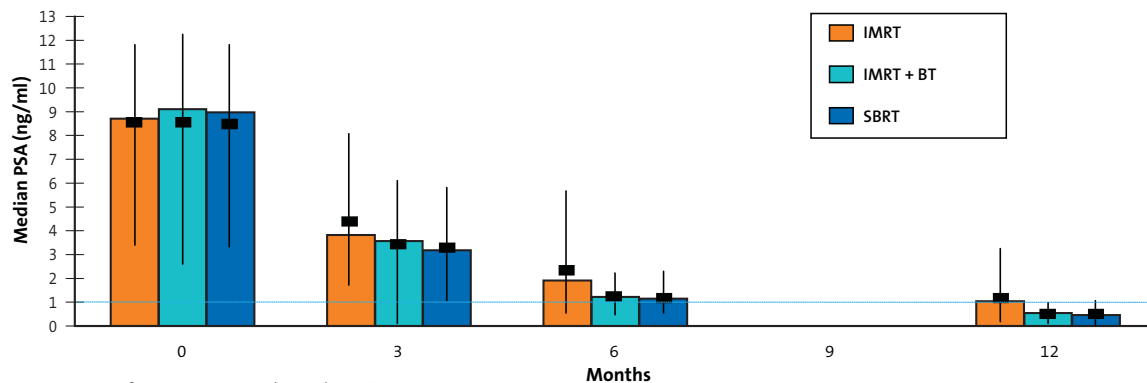
The study from Memorial Sloan-Kettering Cancer Center (MSKCC)<sup>14</sup> yielded a higher PSA control rate and a much lower rectal toxicity rate than the study from M.D. Anderson Cancer Center (MDACC),<sup>13</sup> likely because the MSKCC study used IMRT and the MDACC study did not. Image-guided radiation therapy (IGRT) will have a role as imaging technologies to detect and compensate for organ motion become more widely available. While favorable data exist from several SBRT studies with small patient numbers and short followup, the American Society for Radiation Oncology (ASTRO) recommends that these treatments be performed under Institutional Review Board (IRB)-approved clinical trials until the data matures.<sup>19</sup>

There are no controlled trials for most of the therapeutic choices such as external beam radiation versus surgery, external beam radiation versus IMRT, or external beam radiation versus brachytherapy.<sup>6</sup>

The table on the back shows relative uniformity of results independent of treatment. The data also point to improving biochemical control with increasing biological effective dose (BED), which is a measure of normalized dose based on the tissue. As the incidence of prostate cancer increases, it is expected that refinements of therapy will give better results. Direct comparisons between treatment options are not fully valid as the data are not derived from randomized studies. Most of the chronic toxicities listed for external beam are Grade 2, which can be treated with steroids.<sup>6</sup> Grade 3 toxicities represent a small fraction (0-6% urinary and 0-7% rectal) of chronic toxicities.<sup>11-17</sup>

## PSA Response: IMRT, IMRT+ BT, and SBRT Treatments

3 independent groups: 25 consecutive early-stage prostate patients



Data courtesy of 21st Century Oncology, Plantation, FL

## Treatment Techniques for Early Stage Prostate Cancer

	Treatment	Author	Center	Year Pub.	# of Patients	Median Follow-Up (months)	Dose (Gy) # Fx	Prostate BED [ $\alpha/\beta=1.5$ ] (Gy)	% PSA Relapse	Late Normal Tissue BED [ $\alpha/\beta=3$ ] (Gy)	% Grade 2 + 3 Chronic Urinary Toxicity	% Grade 2 + 3 Chronic Rectal Toxicity
SURGERY	Radical Prostatectomy	Walsh <sup>9</sup>	Johns Hopkins Hospital	1994	995	48	NA	NA	18	NA	8*	1*
	Robotic Prostatectomy	Badani <sup>10</sup>	Henry Ford Hospital	2007	2,766	22	NA	NA	16	NA	ND	ND
BRACHY	High Dose Brachytherapy	Grills <sup>11</sup>	William Beaumont Hospital	2004	65	34	$\frac{38}{4}$	279	2	158	28+4	0+0
	Permanent Seed Implant	Eade <sup>12</sup>	Fox Chase Cancer Center	2008	158	48	$\frac{145}{NA}$	NA	6	NA	19+6	8+0
EXTERNAL BEAM	3D Conformal Radiotherapy	Kuban <sup>13</sup>	M.D. Anderson Cancer Center	2008	151	104	$\frac{78}{39}$	182	22	130	7+3	19+7
	High Dose IMRT	Cahlon <sup>14</sup>	Memorial Sloan-Kettering	2008	478	53	$\frac{86.4}{48}$	190	15	138	13+3	2+1
	Hypo-Fractionated RT	Kupelian <sup>15</sup>	Cleveland Clinic	2007	770	45	$\frac{70}{28}$	187	18	128	4+1	3+1
STEREOTACTIC	SBRT	Madsen <sup>16</sup>	Virginia Mason Clinic	2007	40	41	$\frac{33.5}{5}$	193	30	108	20+0	8+0
	SBRT	King <sup>17</sup>	Stanford University Medical Center	2008	41	33	$\frac{36.25}{5}$	212	0	124	24+5	15+0
	SBRT	Mantz <sup>18</sup>	21st Century Oncology	2008	30	6	$\frac{36.25}{5}$	212	0	124	ND	ND

Biological Equivalent Dose (BED) =  $D * [1 + \frac{d}{\alpha/\beta}]$ , where D = total dose and d = dose per fraction NA: Not Applicable ND: No Data BT: Brachytherapy Gy = Grey = unit of dose Fx = fractions, synonymous with number of treatments \*Walsh did not separate Grade 2 from Grade 3 toxicities

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