Why is Volumetric Modulated Arc Therapy Better Than Three Dimensional Conformal Radiotherapy in Prostate Cancer? Dosimetric Analysis from a Tertiary Care Hospital in Saudi Arabia

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Abstract:

Background: Prostate cancer is one of the most common cancers among older men. It is ranked as the third most common cancer among Saudi men. (As per the last Saudi cancer registry,2016) Current protocols for prostate cancer external beam radiation therapy (EBRT) commonly use two main techniques for treatment planning, including three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT) including volumetric modulated arc therapy (VMAT).

Objectives: The goal of this study is to compare target volumes and organ at risk (OAR) for VMAT versus 3D-CRT plans.

Materials and methods: Forty patients with localized prostate cancer, diagnosed and treated at King Fahad Medical City (KFMC), Riyadh, Saudi Arabia were selected retrospectively for this planning study. Patients were treated with radical definitive external beam radiation therapy (EBRT) using the VMAT technique with a prescribed dose of 78Gy in 39 daily fractions over about 8 weeks. Elective pelvic nodal irradiation was not performed. All patients were re-planned with six fields of 3D-CRT for study purposes. Treatments were delivered using the Trilogy VARIAN Linear Accelerator. Treatment plans were done by Eclipse Varian treatment planning system (TPS) version 10, dose calculations were performed using Analytical Anisotropic Algorithm (AAA) for both VMAT and 3D-CRT techniques. Plans were evaluated using the conformity index (CI) and homogeneity index (HI) for target volumes. Mean, maximum, and OAR dose volumes were compared between both techniques based on QUANTEC normal tissue tolerance doses. Data was analyzed using SPSS-23.

Results: Planning Target Volume (PTV) received a significantly higher maximum dose in VMAT than 3D-CRT plans (p=0.000). The HI for PTV was better in 3D-CRT compared to VMAT plans (p = 0.010). However, CI was significantly better in VMAT vs. 3D-CRT plans (p = 0.002). As expected, 3D-CRT plans required a smaller number of monitor units (MU) than VMAT plans to deliver the same prescribed dose (p = 0.000). VMAT technique resulted in the delivery of lower OAR mean doses to the rectum, penile bulb, bone marrow, and femoral heads compared to the 3D-CRT technique ($p < 0.05$); however, there was no significant difference between the two techniques for small bowel (p=0.234) and bladder (p=0.509). On the other hand, the mean dose was lower in 3D than the VMAT plan for testis (p = 0.000). VMAT delivered significantly higher maximum doses than 3D-CRT to the bladder and rectum while 3D-CRT delivered higher maximum doses to the femoral heads and small bowel. VMAT plans resulted in the delivery of significantly lower OAR dose volumes for all dosimetric endpoints, except for small bowel (V45) and bone marrow (V5), for which there was no significant difference.

Conclusion: VMAT generated more favorable treatment plans compared to 3D-CRT, however, 3-D CRT can also achieve QUANTEC goals with required PTV coverage. VMAT requires more MU than 3 D-CRT, raising the issue of possible second malignancies that need to be clarified by further clinical trials.

Keywords: prostate cancer, radiation therapy, VMAT, 3D-CRT

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Introduction:

Prostate cancer is the most common cancer in men in the United States, and it is about one in eight risk of developing prostate cancer lifetime [1]. Prostate cancer is one of the most common cancers affecting older age groups in Saudi Arabian men. In 2016, the Saudi cancer registry reported prostate cancer as the third most common cancer among Saudi men [2]. Radical prostatectomy and radical radiation therapy, with or without hormonal ablation, are currently considered the standard of care in localized prostate cancer. However, optimal therapy depends on the disease presentation including tumor, node, and metastasis (TNM) staging and established risk factors. Radiation therapy is delivered either as external beam radiation therapy (EBRT), brachytherapy, or a combination [3]. Radiation therapy aims to give the prescribed dose to the tumor and to protect the organs at risk (OAR) and surrounding healthy tissue as much as possible [4]. Current protocols for prostate cancer EBRT commonly use two main techniques for treatment planning, 3D conformal radiation therapy (3D-CRT) and intensity modulated radiation therapy (IMRT) including volumetric modulated arc therapy (VMAT). IMRT (including VMAT) is an advanced technique of high-precision radiotherapy that uses a computer-controlled linear accelerator (LINAC) to deliver accurate radiation doses to a malignant tumor or specific areas within the tumor [5]. VMAT planning is a complex treatment strategy for IMRT and has the same goal as 3D-CRT treatment planning, namely, to treat clinical targets to the most therapeutically effective dose while providing the greatest possible protection for OAR [6]. It is necessary to compare and know the advantages and disadvantages of 3D-CRT and VMAT to choose the right method for every patient. This analysis compares VMAT against 3D-CRT delivery techniques for the treatment of prostate cancer patients in Saudi Arabian men. IMRT allows for the radiation dose to conform more precisely to the three-dimensional shape of the tumor by modulating or controlling the intensity of the radiation beam in multiple small volumes. It also allows higher radiation doses to be focused on regions within the tumor while minimizing the dose to surrounding normal critical structures [7]. Although the processes of VMAT and 3D-CRT techniques are similar, the design plan differs significantly. Conventional 3D-CRT treatment planning is manually optimized. The treatment planner (the dosimetrist) chooses all beam parameters, such as the number of beams, beam directions, shapes, weights, etc., and then the computer calculates the resulting dose distribution. In VMAT, the dose distribution is inversely determined, where the dosimetrist has to decide the dose distribution that he wants beforehand. Then, the computer calculates a group of beam intensities that will be produced, as nearly as possible to the desired dose distribution [4]. Many treatment plans created with IMRT show reduced doses of OAR compared to 3D-CRT plans, including small volumes of OAR at doses higher than the prescription dose and possibly small regions of target at doses lower than the prescription dose; Therefore, it is of clinical interest to know the difference between the two techniques [8]. Over the past few decades, those approaches has seen significant development, allowing for the delivery of a higher radiation dose to the tumor while minimizing harm to healthy tissue and protecting OAR. Innovative advancements in treatment planning, imaging, and delivery have given rise to highly conformal treatments like VMAT and IMRT [9-10].

Patients and Methods:

After obtaining ethical approval, forty patients with localized prostate cancer, diagnosed and treated at King Fahad Medical City (KFMC), Riyadh, Saudi Arabia, were included in the study. All patients who had treatment with radical definitive EBRT using variable dose rate VMAT (vdr-VMAT) technique with no treatment to regional lymph nodes (RLN) were selected randomly and re-planned with 3D-CRT. Exclusion criteria were patients <40 years, patients treated with techniques other than VMAT, or patients who were treated with brachytherapy or surgery. Computed tomography simulation (CT sim) was performed in a supine position with a reasonably full bladder. The prescription dose was 78 Gy over 39 daily fractions over about 8 weeks, delivered to PTV according to International Commission on Radiation Units and Measurements (ICRU) reference point report 62, where ≥ 98% of PTV covered by 95% of the prescribed dose and the aim was to retain the maximum point dose at ≤107%. OAR of our interest in this study included bladder, rectum, bone marrow, small bowel, penile bulb, right femoral head, left femoral head, and testis. Tools used to assess inter-technique preference for coverage of PTV included the Conformity Index (CI), Homogeneity Index (HI), and dose-volume histogram (DVH). OARs were compared based on QUANTEC tolerance doses. Statistical analysis is calculated using means, ranges, and standard deviations. Independent samples t-test was used, and data was entered and processed using SPSS-23. A p-value < 0.05 was considered statistically significant.

Clinical target volumes (CTVs), PTVs, and OARs were contoured as per standard guidelines and reviewed by radiation oncology consultants.

Treatment plans were completed using the treatment planning system (TPS) Varian Eclipse, version 10, and dose calculations were performed using the Analytical Anisotropic Algorithm (AAA) for both 3D and VMAT techniques. Heterogeneity correction was used. VMAT technique was accomplished using a single arc per phase (Starting at a gantry angle of 181° to 179° and rotating counterclockwise), the dose rate was 600, energy 6 MV, using dynamic MLC with a distance of 0.5 mm from PTV (fig.1). 3D-CRT technique accomplished using six fields per phase: four oblique fields with angels of 45°, 135°, 225°, and 315°, and two lateral fields with angels of 90° and 270°, energy 18 MV, weight summation =1, using static MLC with a distance of 0.8 mm from PTV (fig.2). Dose distribution on VMAT plan (fig.3) and 3D-CRT plan (fig.4).

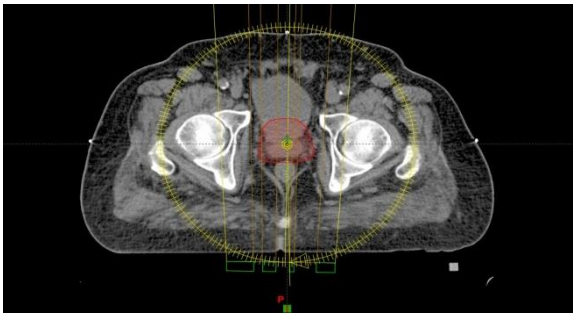

Fig.1 presents an axial computed tomography slice showing the VMAT plan with PTV contoured, the yellow circle indicates the gantry rotation.

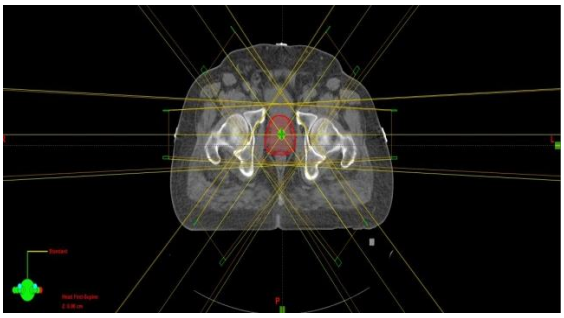

Fig.2 presents an axial computed tomography slice showing a 3D-CRT plan with PTV contoured and six fields.

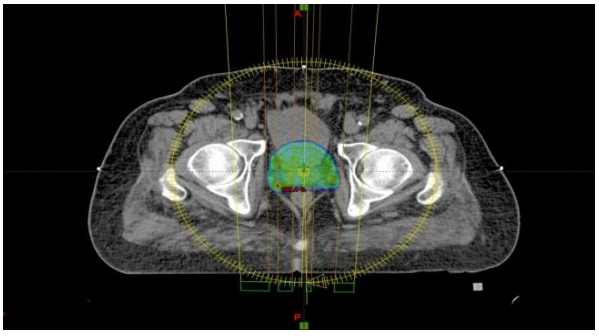

Fig.3 presents an axial computed tomography slice showing dose coverage for the VMAT plan.

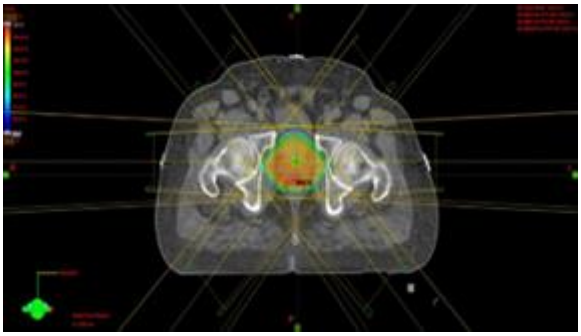

Fig.4 presents an axial computed tomography slice showing dose coverage for the 3D-CRT plan.

Results:

The mean CTV volume for the 40 patients in this study was 66.2 cc (range 20.2 – 331.9), mean PTV volume was 153.9 cc (range 47.7 – 709.3), mean bladder volume value was 296.3 cc (range 78.5 – 802.8), mean rectum volume was 98.2 cc (range 33.7 – 266.8), mean bone marrow volume was 910.8 cc (range 156.7 – 1952.0), mean small bowel volume was 2114.6 cc (range 301 – 7340.9), mean penile bulb volume was 2.4 cc (range 0.9 – 6.6), mean right femoral head volume was 153.8 cc (range 49.9 – 235.6) and the mean for left femoral head volume was 154.3 cc (range 52.3 – 238.1).

A) Target dose coverage and monitor units (MU PTV in VMAT plans received higher maximum and lower minimum doses compared with 3D-CRT plans. CI for the PTV of VMAT techniques was better than 3D-CRT plans ($p = 0.002$) while we found a significant difference in HI for PTV ($P = 0.000$) where dose homogeneity was better in 3D-CRT compared to VMAT. 3D-CRT plans produced a smaller number of MU than VMAT plans to deliver the same dose ($p=0.000$) (tables 1 and 2).

B) Organs at risk (OAR):

1- Bladder: Bladder maximum dose was higher in VMAT plans than 3D-CRT ($p= 0.000$). Volumes that receive 50Gy, 60Gy, 65Gy, 70Gy and 75Gy in 3D-CRT plans were higher than VMAT plans ($p =0.000$). There was no significant difference in mean dose ($p > 0.5$) (table 3).

2- Rectum: There was a significant difference in rectum maximum dose in both plans ($p = 0.000$) which was lower in 3D-CRT plans. Rectum mean dose is higher in 3D-CRT plans than in VMAT plans ($p= 0.000$). Volumes that receive 50Gy, 60Gy, 65Gy, 70Gy and 75 Gy in 3D-CRT plans are higher than VMAT plans ($p = 0.000$) (table 4).

3- Bone marrow: Bone marrow mean dose and volumes that receive 10, 20, 30, 40, 50, 60, and 70 Gy in 3D-CRT plans were higher than in VMAT plans ($p < 0.05$). There was no difference in bone marrow maximum dose ($p = 0.784$) and volume that received 5 Gy ($p = 0.373$) between both techniques (table 5).

4-Small bowel: There was a significant difference in small bowel maximum dose ($p=0.042$) which was better in the VMAT technique, while mean dose and V45 were not significant ($p=0.234$ and 0.126) (table 6).

5-Penile bulb: There was no significant difference in penile bulb maximum dose ($p = 0.163$), but regarding mean dose, D60, D70, D90, and D95 were better in the VMAT technique ($p=0.000$) (table 6).

6-Right and left femoral heads: Right and left femoral head maximum dose, mean dose, V25, and V50 in 3D-CRT plans were higher in 3D-CRT than in VMAT plans ($p=0.000$) (table 6).

7-Testis: There was no significant difference in testis maximum dose ($p = 0.331$), but mean dose was better in 3D-CRT, ($p< 0.000$) (table 6).

Table (1): Comparison between dose coverage of CTV and PTV in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D-CRT		VMAT		
	Mean	S.D.	Mean	S.D.	
CTV Minimum Dose (Gy)	78.21	2.14	75.96	4.00	0.000
CTV Maximum Dose (Gy)	81.50	0.60	83.66	1.35	0.000
CTV Mean Dose (Gy)	80.51	0.38	80.23	0.90	0.069
Dose to 2% of CTV (Gy)	81.27	0.52	81.91	1.10	0.000
Dose to 50% of CTV (Gy)	80.04	3.18	80.31	0.97	0.601
Dose to 95% of CTV (Gy)	79.71	0.40	78.82	1.57	0.002
Dose to 98% of CTV (Gy)	79.43	0.54	78.27	2.64	0.011
Dose to 100% of CTV (Gy)	78.14	2.14	75.96	4.02	0.000
CTV Volume Receiving 95% of Prescribed Dose (%)	100.00	0.02	99.85	0.88	0.288
CTV Volume Receiving 100% of Prescribed Dose (%)	99.80	0.48	95.70	11.49	0.030
CTV Volume Receiving 107% of Prescribed Dose (%)	0.00	0.00	0.86	3.39	0.118
CTV Homogeneity Index	1.05	0.01	1.07	0.02	0.000

Table (2): Comparison between dose coverage of PTV in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D-CRT		VMAT		
	Mean	S.D.	Mean	S.D.	
PTV Minimum Dose (Gy)	74.95	1.84	67.48	6.44	0.000
PTV Maximum Dose (Gy)	81.57	0.65	84.51	1.32	0.000
PTV Mean Dose (Gy)	80.12	0.33	80.04	0.98	0.613
Dose to 2% of PTV (Gy)	81.27	0.53	82.14	1.02	0.000
Dose to 50% of PTV (Gy)	80.09	1.67	80.25	0.95	0.640
Dose to 95% of PTV (Gy)	78.41	0.59	77.44	2.88	0.033
Dose to 98% of PTV (Gy)	77.69	0.78	76.40	3.07	0.008
Dose to 100% of PTV (Gy)	75.03	1.92	67.53	6.42	0.000
PTV Volume Receiving 95% of Prescribed Dose (%)	99.99	0.02	98.96	2.80	0.024
PTV Volume Receiving 100% of Prescribed Dose (%)	96.47	1.89	90.85	12.33	0.006
PTV Volume Receiving 107% of Prescribed Dose (%)	0.00	0.00	0.48	0.98	0.004
PTV Homogeneity Index	1.05	0.01	1.08	0.02	0.000
PTV Conformity Index	1.52	0.37	1.32	0.54	0.002
Monitor Units	13118.53	4580.72	30814.23	11579.65	0.000

Table (3): Comparison between bladder dose constraints in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D-CRT		VMAT		
	Mean	S.D.	Mean	S.D.	
Bladder Maximum Dose (Gy)	80.75	0.73	83.27	1.49	0.000
Bladder Mean Dose (Gy)	36.39	17.38	35.42	13.48	0.509
Bladder Volume Receiving 50 Gy (%)	36.30	22.92	29.49	17.43	0.000
Bladder Volume Receiving 60 Gy (%)	28.86	18.95	21.65	15.19	0.000
Bladder Volume Receiving 65 Gy (%)	25.95	17.99	18.23	14.44	0.000
Bladder Volume Receiving 70 Gy (%)	23.13	17.03	15.66	13.49	0.000
Bladder Volume Receiving 75 Gy (%)	18.74	15.27	12.52	12.12	0.000

Table (4): Comparison between Rectum dose constraints in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D-CRT		VMAT		
	Mean	S.D.	Mean	S.D.	
Rectum Maximum Dose (Gy)	81.26	0.64	82.13	1.38	0.000
Rectum Mean Dose (Gy)	43.66	10.98	34.91	7.00	0.000
Rectum Volume Receiving 50 Gy (%)	50.97	16.51	31.53	11.17	0.000
Rectum Volume Receiving 60 Gy (%)	36.80	15.85	20.59	8.34	0.000
Rectum Volume Receiving 65 Gy (%)	31.38	15.00	15.84	7.45	0.000
Rectum Volume Receiving 70 Gy (%)	26.90	14.41	11.81	6.45	0.000
Rectum Volume Receiving 75 Gy (%)	21.18	13.20	9.21	10.71	0.000

Table (5): Comparison between bone marrow dose constraints in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D-CRT		VMAT		
	Mean	S.D.	Mean	S.D.	
Bone Marrow maximum dose (Gy)	80.16	2.19	79.85	8.60	0.784
Bone Marrow mean dose (Gy)	23.57	8.45	15.75	6.02	0.000
Bone Marrow volume receiving 5 Gy (%)	66.46	24.64	65.58	23.67	0.373
Bone Marrow volume receiving 10 Gy (%)	61.54	23.48	56.09	20.95	0.000
Bone Marrow volume receiving 20 Gy (%)	55.24	21.28	32.56	16.64	0.000
Bone Marrow volume receiving 30 Gy (%)	45.43	17.83	16.39	10.50	0.000
Bone Marrow volume receiving 40 Gy (%)	19.15	9.22	7.57	6.70	0.000
Bone Marrow volume receiving 50 Gy (%)	13.13	7.72	3.54	3.47	0.000
Bone Marrow volume receiving 60 Gy (%)	4.45	4.69	1.75	1.82	0.000
Bone Marrow volume receiving 70 Gy (%)	2.74	3.21	0.93	1.25	0.000

Table (6): Comparison between small bowel, penile bulb, femoral heads, and testis dose constraints in 3D-CRT and VMAT techniques

	Radiotherapy Technique				*P value*
	3D		RA		
	Mean	S.D.	Mean	S.D.	
Small bowel maximum dose (Gy)	37.66	24.56	33.19	22.27	0.042
Small bowel mean dose (Gy	2.48	4.17	3.11	4.45	0.234
Small bowel volume receiving 45 Gy (%)	1.81	4.69	0.56	2.33	0.126
Penile bulb maximum dose (Gy)	73.98	10.11	71.42	17.92	0.163
Penile bulb mean dose (Gy)	58.84	17.75	47.64	20.02	0.000
Dose to 60 % of penile bulb (Gy)	56.54	21.16	42.10	23.42	0.000
Dose to 70 % of penile bulb (Gy)	52.60	22.37	36.47	24.22	0.000
Dose to 90 % of penile bulb (Gy)	43.76	23.08	27.73	23.11	0.000
Dose to 95 % of penile bulb (Gy)	42.02	22.96	26.23	22.61	0.000
Rt. femoral head maximum dose (Gy)	63.30	11.51	37.85	10.35	0.000
Rt. femoral head mean dose (Gy)	28.92	5.93	16.68	5.66	0.000
Rt. femoral head volume receiving 25 Gy	73.36	16.28	17.96	21.20	0.000
Rt. femoral head volume receiving 50 Gy	7.86	8.90	0.08	0.43	0.000
Lt. femoral head maximum dose (Gy)	62.37	12.68	38.17	10.55	0.000
Lt. femoral head mean dose (Gy)	28.66	6.11	16.56	5.63	0.000
Lt. femoral head volume receiving 25 Gy	72.77	18.27	16.55	21.30	0.000
Lt. femoral head volume receiving 50 Gy	7.11	8.78	0.07	0.23	0.000
Testis maximum dose (Gy)	4.14	13.86	2.97	7.67	0.331
Testis mean dose (Gy)	0.61	0.30	0.90	0.42	0.000

Discussion:

This study was done at the Radiation Oncology department, KFMC, Riyadh, in collaboration with Princess Nora University Riyadh to help the therapist graduates to understand different modalities of treatment used in radiation. We chose this point to compare statistically between the two common modalities of treatment we had at that time. We tried to add more (OAR) e.g., testis and bone marrow to check the scattered and low dose effect of both modalities on these organs (needed to be clinically correlated in future studies). VMAT technique is one of the more recent techniques in radiation therapy and has proved a better dose distribution compared to 3D-CRT in many treatment planning studies involving localized prostate cancer, delivering lower doses to OARs while maintaining an adequate dose to the target. Our results for the dose coverage are comparable with those reported by Palma et al., 2008 [11], Wolff et al.,2009 [6], and Adam et al., 2012 [5], in which conformity to PTV is better in VMAT than 3D-CRT. However, in our study, VMAT showed slightly less dose homogeneity than 3D-CRT. This study agrees with Palma et al., 2008 [11] and Wolff et al., 2009 [6] in which PTV in VMAT received a higher maximum dose and lower minimum dose compared to 3D-CRT. Although in Hoffman et al., 2019, they were comparing between IMRT and VMAT but they found comparable HI for both methods, suggesting that the dosage distribution in the target volume was similarly uniform with better CI, however, was seen for VMAT in comparison to IMRT plans [10]. The doses to the OARs were lower in VMAT than 3D CRT technique and that was also shown in Gozal et al.,

2021 in which the VMAT technique was considered capable of escalating dose to prostate cancer patients and minimizing toxicity to the rectum and bladder [12]. Our results are consistent with previous dosimetric studies that showed a similar or greater sparing to OARs with VMAT as compared to prostate IMRT plans by Hoffman et al., 2019 particularly when using the dual-arc approach [10]. Based on these findings, we can safely use the VMAT technique for localized prostate cancer. Nonetheless, VMAT required a larger number of MU than 3 D-CRT, which may raise more attention to the induction of second malignancies [5,6, and 11]. Recently we had a new helical tomotherapy machine, hopefully to have a comparison between the three modalities in future studies.

Conclusion:

In treatment planning for prostate cancer, VMAT produces more favorable dose distributions than those achieved by 3D-CRT. However, 3-D CRT can achieve QUANTEC goals with required PTV coverage. VMAT requires more MU than 3 D-CRT, raising the issue of possible second malignancies. Clinical trials are needed to determine whether the improved dose distribution with VMAT results in decreased toxicity, more organs at risk should be evaluated and long-term follow-up would be required to determine the potential for VMAT to decrease the rate of secondary malignancies compared to 3D-CRT.

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