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Review Article

Volumetric Modulated Arc Therapy versus Intensity Modulated Radiation Therapy in the Treatment of Prostate Cancer: A Systematic Literature Review

Abstract

Aim: provide evidence concerning advantages of volumetric modulated arc therapy over intensity modulated radiation therapy.

Background: external beam radiation therapy is a major treatment modality of prostate cancer; especially in high and intermediate risk categories in combination with androgen deprivation therapy. The advent of new techniques of irradiation such as intensity modulated radiation therapy (IMRT) improved significantly the biochemical free survival by allowing dose escalation without enhancement of related toxicities. Volumetric modulated arc therapy (VMAT) is a circular technique delivering radiation dose using one or multiple arc of 360° around the target volumes.

Methods: We collected all dosimetric studies comparing VMAT versus IMRT, published in PubMed indexed journals between 2008 and 2015. Parameters of comparison were dose volume histograms for target volumes and organs at risk, number of monitor units and treatment time.

Results: Globally, the target volumes coverage and organ at risk protection were similar between the two techniques. VMAT has the advantage to reduce significantly the number of monitor units and treatment time.

Conclusion: VMAT is a very efficient technique of radiation therapy, and should be preferred in the treatment of prostate cancer.

Background

Prostate cancer is the leading cancer in men after the age of 50; he is a real public health problem. According to the data of 2005 cancer registry of the Rabat region (RECRAB), prostate cancer is the second most common cancer in men after lung cancers with standardized incidence to the world population of 23,3/100000 inhabitants. US data from the SEER program show a ten-years relative survival of 91.7 %. The relative five-years survival is 100 % for localized (80% of diagnoses) and loco regional (12 % of diagnoses) stages, and 30.6 % for metastatic disease [1].

External beam radiation therapy is indicated in the treatment of low-risk patients, with results comparable to surgery and brachytherapy [2]. It also has a place in treating intermediate-risk forms where it can be combined with short androgen therapy (3 to 6 months) [3-5], and high-risk patients combined to 2-3 years androgen therapy [6]. The benefit of dose escalation has been proven by several randomized trials, showing a better disease-free survival with high doses radiation (74-80 Gy) compared to conventional radiation doses (68 to 70Gy) [7-12]. This dose escalation was made possible by the advent of new radiation techniques such as IMRT, allowing concave dose distributions around target volumes while sparing the rectum and bladder [13-17]. Dosimetric comparison between IMRT and

3D conformal radiation therapy shows a significant decrease in the dose in the rectum and bladder with improved conformation to the target volumes [18,19]. IMRT typically uses five to seven static fields converging towards an isocenter located at the target volume, and the inverse planning system allow by introducing different constraints dose/volume, a very optimized dose distribution [20]. In IMRT technique by static beams, motion of the MLC leaves may occur continuously (sliding window technique) or sequentially (step and shoot technique) [21,22]. The term VMAT or volumetric modulated arc therapy was introduced for the first time in 2008 by Karl Otto, to designate a new circular irradiation technique, which is the evolution of the intensity modulated arc therapy (IMAT) introduced by Yu in 1995 [23]. A displacement of the MLC leaves with variable speed, a rotational displacement of the gantry with variable speed, a variation of the dose rate and a rotation of the collimator, characterize VMAT technique.

Data on the potential benefits of VMAT compared to IMRT are few. Our work proposes through a systematic literature review to collect all the comparative studies published. Three types of comparison criteria will be discussed:

- Criteria related to the target volumes coverage and protection of organs at risk

- Efficiency criteria
- Economic criteria

Methods

The literature search was conducted by the systematic interrogation of the Pub Med database from 2008 to 2015, the key words used were: Volumetric modulated arc therapy (VMAT) versus Intensity modulated radiation therapy (IMRT), dosimetric comparison, prostate cancer. The literature search was limited to publications in English or French. Studies presented as abstracts or oral presentation in international conferences but not published were excluded.

The studied comparisons were: VMAT (SA = single arc, DA = Double arc, CDR = constant dose rate, VDV = variable dose rate) versus IMRT (SW = sliding window or SS = Step and shoot).

The comparison parameters were:

- Dose Volume Histograms for PTV
- Dose Volume Histograms for OAR
- Number of monitor units
- Treatment time.

Results

29 dosimetric studies met our selection criteria; their results are summarized in **Table 1**. In general VMAT and IMRT have provided similar coverage of target volumes while respecting the constraints for organs at risk. The number of monitor units and treatment time were significantly reduced with VMAT.

Discussion

A-Coverage of target volumes

In all published dosimetric studies, VMAT technique has allowed coverage of target volumes, acceptable and comparable to that provided by conventional IMRT using fixed or stationary fields. However, the results concerning homogeneity and conformity are more controversial, since some studies report better homogeneity and conformity with VMAT [31,34], while others are more in favor of IMRT [32,36]. It is important to remember that these differences rather insignificant are inherent to many factors:

- The number of arcs used in VMAT treatment plans (usually with better homogeneity and improved conformity with multiple arcs)
- The optimization method used for VMAT plans
- The number of beams used for IMRT, a high number of beams generally allows better results [31,32]
- Expertise of the radio physics team

B-Protection of organs at risk

In the study of Palma et al. [24], as well as VMAT and IMRT resulted in a significant reduction of the dose to OAR compared to 3D conformal radiation therapy, these doses were lowest with VMAT. The comparative study of the Memorial Sloan Kettering Cancer Center [25], reported a significant reduction of the dose to the rectum and the rectum-NTCP by 1.5%, the doses to the bladder and the femoral heads were also reduced but not significantly. Similar results were reported by Hardcastle et al. [26], with reduced doses to the rectum and therefore a lower rectum-NTCP with VMAT versus IMRT (7F, SS). In a Danish study [27], the VMAT technique has reduced doses

Table 1: Results of dosimetric studies comparing VMAT and IMRT in prostate cancer.

Article	PTV	OAR	MU number	Treatment time per fraction (min or second) or total (hour)
Palma et al. [24]	Similar PTV coverage and homogeneity	VMAT - VDR better than IMRT (sparing of the rectum and femoral heads), and VMAT- CDR (sparing of the bladder and rectum)	VMAT- CDR: 491.6; VMAT-VDR: 454.2; IMRT: 788.8	
Zhang et al. [25]	IMRT: PTV dose slightly higher, Better homogeneity over VMAT	VMAT better than IMRT (better protection of the rectum, bladder, femoral heads)	VMAT: 290; IMRT: 642	VMAT 1min, IMRT 5 min
Kjaer et al. [26]	IMRT slightly better for coverage of PTV (V95 %) but VMAT is better for the coverage of volume (PTV- rectum). Higher hot spots in VMAT Plans	VMAT better than IMRT (better protection of the rectum, bladder).	VMAT: 529; IMRT: 647	
Hardcastle et al. [27]	Similar PTV coverage	VMAT: better protection of the rectum, but higher doses to femoral heads.	VMAT: 417; IMRT: 526	VMAT 1,3 min, IMRT 4,5 min
Ost et al. [28]	Similar PTV coverage	VMAT better protection of the rectum	VMAT: 447; IMRT 3F: 362; IMRT 5F: 407; IMRT 7F: 434	VMAT: 1,95 IMRT 5F: 3,85 IMRT 7F: 4,82
Weber et al. [29]	VMAT: better than IMRT for coverage of GTV and PTV, Better homogeneity	VMAT better than IMRT (protection of the rectum, urethra, bladder)		
Kopp et al. [30]	Similar PTV coverage IMRT: better homogeneity	VMAT better to protect the rectum (for high doses) , femoral heads, bladder, penile bulb		

Yoo et al. [31]	Initial plans: IMRT better Boost: similar PTV coverage and homogeneity, better conformity with VMAT	Initial plans: IMRT better than VMAT (PTV coverage, conformity) Boost plans: similar PTV coverage and homogeneity. Better conformity with VMAT	Initial plans: VMAT SA 429; VMAT DA 444; IMRT1300 Boost plans: VMAT SA 443; VMAT DA 484; IMRT 777	Initial plans: VMAT SA 1.5 min, VMAT DA 3.1 min, RCMI 8.1 min Boost plans: VMAT SA 1.5 min, VMAT DA 3.1 min, IMRT 4.9 min
Wolff et al. [32]	Best PTV coverage with VMAT Better conformity with IMRT Similar homogeneity	IMRT better than VMAT for rectal protection	VMAT (SA) 386; VMAT (DA) 371; IMRT 544	VMAT (SA) 1.8 min, VMAT (DA) 3.7min, IMRT 6 min,
Tsai et al. [33]	Similar PTV coverage	Similar protection of OAR, VMAT slightly better for rectal protection	VMAT 309.7; IMRT 336	VMAT 2.6 min, RCMI 3.8 min,
Rao et al. [34]	Similar PTV coverage Best conformity with VMAT	Similar protection of OAR	VMAT 549; IMRT 639	VMAT 2.2 min, IMRT 8.1 min,
Shaffer et al. [35]	Similar PTV coverage		VMAT 949; IMRT 1819	VMAT 3.7 min, IMRT 9.6 min
Crijns et al. [36]	Similar PTV coverage Better homogeneity with IMRT	Similar protection of OAR		
Guckenberger et al. [37]	Similar PTV coverage Better conformity with VMAT DA	VMAT slightly better for the protection of the rectum and bladder	VMAT (SA) 465; VMAT (DA) 572 ; IMRT 513	VMAT (SA) 2.08 min, VMAT (DA) 3.87 min, IMRT 5.82 min
Fontenot et al. [38]	Similar PTV coverage and homogeneity	Similar protection of OAR	- prostate plan : 20 % less MU (p = 0.01) -prostate and pelvis plan : VMAT 45 % less MU (p < 0.01)	Prostate plan: VMAT 1,4 +/- 0,1 min vs IMRT 9,5 +/- 2,4 min (p < 0,01) Prostate and pelvis plan: VMAT 1,4 +/- 0,1 min vs IMRT11,7 +/- 1,3 min (p < 0,01)
Davidson et al. [39]	Similar PTV coverage	Similar protection of OAR	15-38 % with VMAT	75% (70-86%) with VMAT
Aznar et al. [40]	Similar PTV coverage	VMAT better for rectal protection, IMRT better for femoral heads protection	VMAT 452+/- 77 vs IMRT 657 +/- 217 (p<0.0001)	VMAT 1.08+/- 0.05 (1.03-1.23) ; IMRT 4.87 +/- 1.31 (3.40-8.92) (p<0.0001)
Morales-Paliza et al. [41]	Similar PTV coverage	Similar protection of OAR	VMAT 319+/- 35 vs IMRT 966 +/-235	
Jouyaux et al. [42]	V77 and V80 Gy significantly increased with VMAT (p < 0.05)	Nonsignificant trend to a decrease in the dose to organs at risk with VMAT	8% reduction with VMAT	VMAT 1.95 min vs IMRT 4 min
Sale C, et al. [43]	Similar PTV coverage	Similar protection of OAR		
Fogarty et al. [44]			IMRT: 1813.9 VMAT : 590.2 (p <0.001)	IMRT : 5.2 h VMAT: 3.1 h (p= 0.001)
Leszczynski, et al. [45]	Radiation planning index better with IMRT	Radiation planning index better with IMRT	VMAT: 442 vs IMRT: 809	45% reduction with VMAT
Sze et al. [46]	VMAT DA: highest minimum PTV dose, lowest hotspot, best homogeneity and conformity.	Highest rectal doses with VMAT SA	IMRT : 864 VMAT DA :702 VMAT SA : 584	IMRT : 4.80 min, VMAT SA : 2.78 min, VMAT DA :1.30 min
Ishii et al. [47]	VMAT: slightly superior conformity and homogeneity of prostate PTV	Similar protection of OAR	IMRT 9F : 2588 IMRT 7F :2383 VMAT : 526	IMRT 9F : 865 s IMRT 7F : 737 s VMAT : 171 s
Elith et al. [48]	IMRT: better homogeneity VMAT: better conformity	VMAT better sparing of OAR	IMRT : 594 VMAT SA : 446.5 VMAT DA : 450.5	IMRT : 3.14 VMAT SA : 1.3 VMAT DA : 3.18
Poon et al. [49]	VMAT: better conformity and better homogeneity for PTV boost	Similar OAR protection	VMAT : reduction by 60.93% for initial PTV and 48.06% for PTV boost,	VMAT : reduction by 74.09%for initial PTV and 68.32%for PTV boost,
Kinhikar et al. [50]	Similar PTV coverage	Similar OAR protection	IMRT 942 VMAT 581	IMRT 2.36 VMAT 1.45
Peters et al. [51]	Similar PTV coverage Better conformity with VMAT	Similar OAR protection VMAT: smaller maximum dose to the rectum	VMAT: reduction by 31%	
Riou et al. [52]	IMRT : better homogeneity for PTV boost	VMAT : higher Doses to femoral heads	IMRT 1297 VMAT 512s	

CDR: constant dose rate, VDR: variable dose rate, DA: Double arc, SA: single arc, F: field.

to the rectum and bladder compared to IMRT (SW). Ost et al. [28], have compared VMAT with three techniques of IMRT (3F, 5F, 7F-SS), for prostate radiotherapy with a simultaneous integrated boost to the intraprostatic lesion defined by MRI spectroscopy, VMAT in this study compared to the three IMRT techniques has reduced the dose to the rectum, this reduction was statistically significant for the volumes receiving doses between 20 and 50 Gy ($p < 0.001$). In Weber et al. study [29], comparing VMAT with IMRT (5F, SW) and proton therapy for recurrent prostate cancer after radiation therapy, VMAT and proton therapy allowed a better sparing of OAR compared to IMRT. In a study of 292 patients, the mean doses to the rectum and bladder were lower with VMAT compared with IMRT (7F, SW), especially in the volumes of high doses [30]. However, the results of many studies have shown that IMRT allow a better OAR sparing compared to VMAT [31-34].

C-Peripheral Lower doses or bath doses

The results of comparative studies concerning the integral dose are conflicting, some studies show no difference between the two techniques [26,28], while others report higher levels of whole body integral dose with VMAT compared with IMRT [31]. This difference would be the fact that the full dose, do not depend only on the number of MU, but also significantly on the size of the target volume, shape and dimensions of the opening of the collimator. It is important to note that the dose distributions obtained by VMAT compared with IMRT, generally show higher volumes receiving low doses in the periphery, this is due to the fact that VMAT dose is delivered on an entire 360 degree arc. However, the increased conformity obtained with intensity modulation techniques including VMAT, reduces high doses in healthy tissue outside the target volume [53].

D-Number of Monitor Units (MU) and treatment time

In published dosimetric studies, VMAT treatment plans generally use less MU (up to 65 % less) compared to IMRT by stationary fields (SS and SW) [25,26,31]. This significant reduction in the number of MU theoretically reduce the whole body integral dose, with consequently less risk of radiation induced carcinogenesis and thus second cancers, which represents the major concern with any technique of modulation of intensity, however, data on the whole body integral dose are contradictory, especially since it does not depend uniquely on the number of MU.

Prolongation of the treatment time has been identified as one of the major drawbacks of conventional IMRT with stationary fields. In some locations, the time required to deliver a fraction of a complex IMRT plan can go beyond 15-30 min [54-56]. This disadvantage has often been accepted as an inevitable consequence of the high conformation to the target volume provided by IMRT. The prolongation of the treatment time has several negative consequences:

- At the institutional level: limitation of the number of patients who can be treated by treatment unit.
- Patient discomfort with increased risk of movement of the tumor or the patient during treatment [57].
- Increased machine time required for quality assurance of complex IMRT plans.

- In radiobiological point of view: some authors have suggested that increasing the treatment time, allow tumor cells to repair radio-induced DNA damages and then their proliferation [58,59].

Thus the major impact of the reduction in the number of MU, is probably the significant reduction of the treatment time that passes from 1-1.5 min with a VMAT plan to 5-10 minutes with IMRT plan with 5-7 beams [35, 60-62], the reduction in treatment time allow not only to treat more patients, but also to treat them with more comfort and less intra-fraction tumor as well as organs at risk movements including bladder and rectum.

E-Economic advantage

Reducing both the number of MU and treatment time, implies a cost reduction related to VMAT technique. This hypothesis has been validated by an Australian study, which demonstrated that the technique of VMAT saves on average 174 DAU per patient, compared to IMRT, which is equivalent to a reduction of the cost of about 34%. Indeed, the real economy is much greater, since only the cost related to the nursing staff has been calculated in this study, not the additional cost related to time and to administrative and nursing staff needed to maintain the activity of radiotherapy department with treatments as long as those of IMRT, nor the logistics cost for the construction of new buildings and installation of new machines to treat the same number of patients in a timely manner. According to the same study, VMAT is logistically and economically equivalent to the RC-3D, with the dosimetric advantages of IMRT [44].

Conclusions

Results of dosimetric studies comparing IMRT and VMAT, should be interpreted with caution, given the number of bias, including the expertise of the radio physics team, the dosimetric advantage of one technique over the other may simply be due to a long learning curve of the medical physicist, which allows him an important mastery of technique, by against, treatment plans made by a team at the beginning of learning naturally suffer of many imperfections, incorrectly deducted to the technique.

Thus at the current state of knowledge, we cannot decide on the superiority of one technique over the other for coverage of target volumes and protection of organs at risk. However, the most plausible benefits of VMAT compared with IMRT are obviously the significant reductions in the number of MU and treatment time, with all the impact that can have:

- Patient comfort.
- The comfort of the healthcare team.
- Treatment accuracy by reducing per fraction movements.
- Reducing the cost of treatment.
- The treatment of more patients in optimal time.

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