Dosimetric comparison of Intensity-modulated radiotherapy versus 3D conformal radiotherapy in patients with prostate and pancreatic cancer

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Abstract

Purpose: This work aimed to develop the best IMRT optimization parameters for prostate and pancreatic cancer and to compare target dose distribution and dose to normal tissue using 3-dimention conformal radiotherapy and intensity modulated radiation therapy (IMRT).

Methods: twelve patients with prostate and ten with pancreatic cancer were chosen to studding the impact of IMRT on the planning target volume coverage and the dose reduction for organ at risks. 3-dimention conformal radiotherapy (3DCRT) and intensity modulated radiation therapy (IMRT) plans were performed for each patient. To evaluate the different treatment plans the dose volume histograms (DVH) for PTV and OARs were used. The homogeneity index (HI) used for evaluation of the dose homogeneity in the target volume.

Results: IMRT has better coverage with a significant P value = 0.0203. Homogeneity index values for IMRT versus 3D-CRT were 10±2.061 and 8±2.215 respectively, median and standard deviation(STD) for PTV5% for IMRT plans was 105.65±1.360 and this was higher than conformal plans 103±1.311, with highly significant(P= 0.0002). The doses to the rectum and bladder from IMRT-plans were lower than that for 3DCRT-plans which considered very significant also the femoral heads doses were decreased with IMRT compared to 3-DCRT. The comparison results of pancreas cases for PTV coverage and HI were not significant in both plans.

Conclusions: The results showed superior PTV coverage and dose reduction to OAR with IMRT plan comparing to 3D-CRT in prostate cases, IMRT technique enables significant increase in dose homogeneity in the PTV while allowing significant reduction in the doses received by the rectum, bladder and femoral head compared 3DCRT. In pancreatic cases the difference was not significant for PTV coverage and dose to OARs in both plans IMRT and 3DCRT. It's better to use IMRT for prostate cancer to achieve good dose escalation but for the pancreatic patients no need to use the complicated IMRT technique.

1. Introduction

Modern radiation therapy (RT) techniques, including (IMRT) and (3D-CRT), can improve dose conformity to the target volumes, allowing a higher dose delivered to the tumor and reducing the dose to the surrounding normal structures, thus the
rate of a acute and late reaction can be significantly reduced (Xiyin Guan et al., 2013).

Three-dimensional conformal radiation therapy is a technique designed to deliver prescribed radiation doses to localized tumors with high precision, with the help a multi leaf collimator (MLC) to effectively exclude the surrounding normal tissues. In 3D-CRT, the MLC is set to shape the radiation fields using various angles (gantry angles) to conform to the tumor or planning target volume (PTV), and the dose weighting is then adjusted in a trial and-error fashion to refine the plan (Mohamed Metwaly et al., 2008).

IMRT is a highly conformal treatment modality that is used when conventional methods of radiotherapy cannot deliver a tumor dose without exceeding critical structure tolerance (Cozzi et al., 2001; De Neve et al., 1999; Hurkmans et al., 2002; Verellen et al., 1997)

Two major points define the IMRT technique in comparison to 3D-CRT: modulation of the fluence profile and inverse treatment-planning process. Two techniques are routinely applied for modulation of the fluence within the field: dynamic movement of leafs during irradiation sliding window and superposition of multiple irregular, static fields step and shoot. For the step-and-shoot technique the number of intensity levels and consequently the number of segments are important parameters influencing the quality of the dose distribution. However, treatment time increases with increasing number of intensity levels. With the use of about five to ten intensity levels there seems to be no difference between treatment plans calculated for sliding-window and step-and-shoot technique (Chui et al., 2001; Court et al., 2005; De Boer., 2005; De Meerleer et al., 2000; Dogan, King Set al., 2003; Fowler et al., 2005; 2004; Ghilezan et al., 2004; Grosu et al., 2006; Grosu et al., 2005; Guckenberger and Meyer et al., 2006; Guckenberger and Pohl et al., 2006; Kupelian and Potters et al., 2004; Kupelian and Thakkar et al., 2005; Lee et al., 1996; Leibel et al., 1984; Letourneau et al., 2005; Li X.A. et al., 2005; Ling and Burman et al., 1996; Ling and Humm et al., 2000; Litzenberg et al., 2005; 2006; Longobardi et al., 2005; Matthias Guckenberger et al., 2007)

IMRT allows the possibility of producing concave dose distributions and providing specific sparing of normal tissue. Cancer of the prostate is the second most common malignancy in males. Radiotherapy plays an important role in the management of this disease, and the reduction of radiotherapy-associated early and late morbidity assumes high priority. With the recent improvements in radiotherapeutic techniques more patients are cured with only minor chronic morbidity (Galalae et al., 2004; Goldner et al., 2003; Sanguineti et al., 2003).

Intensity-modulated radiation therapy (IMRT) has been shown to decrease toxicity by reducing the radiation dose to critical structures in the upper abdomen, including the kidneys, stomach, and small bowel. One concern regarding the utilization of IMRT in this patient population is the possibility for geographic miss secondary to the increased conformity of the IMRT-based treatment plans and consequent higher risk of local failure (Susannah Y. et al., 2012)

1.1 Justification of Research
There is no well established constrains and IMRT optimization parameters for prostate and pancreatic cancer. This work aimed to develop the best IMRT optimization parameters for prostate and pancreatic cancer.

2. Materials and Methods

Objective of Research
Inverse treatment planning (ITP) for patient undergoing radiotherapy still needs great efforts from the medical physicists to perform the state of the art radiotherapy. Increasing number of beams in IMRT without good optimizations will increase normal tissue doses and so the risks of secondary malignances. This work aimed to develop the best IMRT optimization parameters for prostate and pancreatic cancer.

Twelve patients with prostate and ten with pancreatic cancer were chosen to studing the impact of IMRT on the planning target volume coverage and the dose reduction for organ at risks. 3-dimention conformal radiotherapy (3DCRT) and intensity modulated radiation therapy (IMRT) plans were performed for each patient.

2.1 Treatment planning system
Computerized Medical Systems (CMS) Inc.’s (St. Louis, MO) XiO software release 4.64 which is a three-dimensional treatment planning system that incorporates modern dose calculation algorithms for dose calculation was used to plan cancer patients; 3DCRT plans and IMRT plans were compared in all cases. The same contours for tumors and organs used to perform plans. The planning strategy in all cases was to achieve the clinical IMRT constraints for the PTV or CTV as much as possible .3dmention radiotherapy plans with 6 and 15 MV photons were generated using the same treatment planning system. Dose volumetric histograms (DVHs) were obtained for each of these plans.
Figure 1: median and standard deviation (SD±) Dose % Received by 95% of PTV for IMRT and 3DCRT in twelve patients with prostate cancer

Figure 2: median and standard deviation (SD±) for homogeneity index (HI) for IMRT and 3DCRT in twelve patients with prostate cancer

Figure 3: median and standard deviation (SD±) Dose % Received by 5% of PTV for IMRT and 3DCRT in twelve patients with prostate cancer
Figure 4: DVH for PTV for IMRT dashed line, and 3DCRT solid line

Figure 5: DVHs for rectum (red), bladder (orange), LT femoral head (light-green), RT femoral head (light-red). IMRT dashed lines and 3DCRT solid lines
Figure 6: Dose distribution in a patient with prostate cancer (a); axial (b); sagittal and (c) coronal view. Left: 3D conformal technique and Right: IMRT. (Blue wash) represents the growth tumor volume (GTV), (green wash) represents PTV, (light red) represents RT fumer, (Light green) represents LT fumer, (orange) represents bladder and (dark red line) represents rectum. Blue isodose line represents 95% of prescribed dose.
Figure 7: mean and SD (±) for PTV98% in IMRT and conformal in ten patients with Pancreas tumor

Figure 8: mean and SD (±) for PTV2% in IMRT and conformal in ten patients with Pancreas tumor

Figure 9: mean and SD (±) for HI in IMRT and conformal in ten patients with Pancreas tumor
Figure 10: Dose volume histograms for PTV with conformal (dashed line) and IMRT (solid line).

Figure 11: Dose volume histograms for OARs with IMRT (dashed line) and conformal (solid line).
**Figure 12:** Dose distributions of 3DCRT and IMRT in three CT slices of a patient with pancreas cancer a) axial, b) coronal, and c) sagittal. Tumor (magenta), right kidney (red line), left kidney (green line) and liver (cyan). The blue line represented 95% of prescribed dose of tumor.

**Figure 13:** Mean and SD of max dose% for spinal cord with 3DCRT and IMRT in ten patients of Pancreas tumor.
Figure 14: mean and SD for integral dose of spinal cord with 3DCRT and IMRT in ten patients of Pancreas tumor

Figure 15: mean and SD (±) for V33% of liver with 3DCRT and IMRT in ten patients with Pancreas tumor

Figure 16: mean and SD (±) for V50% of liver with 3DCRT and IMRT in ten patients with Pancreas tumor
Figure 17: mean and SD (±) for V66% of liver with 3DCRT and IMRT in ten patients with Pancreas tumor

![Graph showing mean and SD for V66% of liver volume with IMRT and Conformal]

Table 1: median and SD (±) of dose% delivered to different volumes of OARs with IMRT and 3DCRT

<table>
<thead>
<tr>
<th>OAR</th>
<th>3DCRT</th>
<th>IMRT</th>
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<tbody>
<tr>
<td></td>
<td>Median</td>
<td>SD</td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose %V15%</td>
<td>95.50</td>
<td>13.65</td>
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<tr>
<td>Dose %V25%</td>
<td>87.5</td>
<td>13.65</td>
</tr>
<tr>
<td>Dose %V35%</td>
<td>78.40</td>
<td>13.73</td>
</tr>
<tr>
<td>Dose %V50%</td>
<td>68.50</td>
<td>17.65</td>
</tr>
<tr>
<td>Bladder</td>
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<td></td>
</tr>
<tr>
<td>Dose %V15%</td>
<td>93.59</td>
<td>11.66</td>
</tr>
<tr>
<td>Dose %V25%</td>
<td>90</td>
<td>19</td>
</tr>
<tr>
<td>Dose %V35%</td>
<td>76</td>
<td>25.65</td>
</tr>
<tr>
<td>Dose %V50%</td>
<td>57</td>
<td>30.77</td>
</tr>
<tr>
<td>Femoral head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose %V10%</td>
<td>52.38</td>
<td>13.45</td>
</tr>
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</table>

Table 2: mean and SD of segment numbers, monitor unit and treatment delivery time

<table>
<thead>
<tr>
<th>Feature</th>
<th>IMRT(mean)</th>
<th>3D-CRT(mean)</th>
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<tbody>
<tr>
<td>Number of beams</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Number of segment</td>
<td>58.89±15.37</td>
<td>4</td>
</tr>
<tr>
<td>Monitor unit</td>
<td>555.44±212.29</td>
<td>285.67±60.60</td>
</tr>
<tr>
<td>Treatment time(sec)</td>
<td>400.42±215.14</td>
<td>279.15±61.66</td>
</tr>
</tbody>
</table>

Table 3: Mean and SD and Integral dose for both kidneys with IMRT & 3DCRT

<table>
<thead>
<tr>
<th>OAR</th>
<th>IMRT</th>
<th>3D-conformal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mea</td>
<td>SD</td>
</tr>
<tr>
<td>Right Kidney</td>
<td>Dose %V33%</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Dose %V50%</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Dose %V66%</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Integral dose</td>
<td>1.49</td>
</tr>
<tr>
<td>Left Kidney</td>
<td>Dose %V33%</td>
<td>17.4</td>
</tr>
<tr>
<td></td>
<td>Dose %V50%</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>Dose %V66%</td>
<td>6.34</td>
</tr>
<tr>
<td></td>
<td>Integral dose</td>
<td>1.34</td>
</tr>
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2.2 Prostate cancer

Twelve patients with localized prostate cancer were studied. Patients underwent computed tomography planning were positioned supine with a slice spacing of 2 mm. The prostate PTV had been delineated 1 cm around the prostate gross target volume (GTV) except in the posterior direction where a 0.5 cm margin was used to spare the rectum, whereas, the bladder, rectum, and femoral head were outlined as the OARs on each CT image. Each patient received a PTV dose of 76 Gray(Gy) in 38 fractions. The dose constraints of organs at risk followed the dose guidelines designed by the Radiation Therapy Oncology Group (RTOG) for patients being treated for localized prostate cancer under RTOG protocol 0126 [36]. The rectal criteria in the RTOG guidelines require no more than 15%, 25%, 35%, and 50% of the rectum volume
should receive more than 75 Gy, 70 Gy, 65 Gy, and 60 Gy respectively. The bladder criteria in the guidelines require no more than 15%, 25%, 35%, and 50% of the bladder volume should receive more than 80 Gy, 75 Gy, 70 Gy, and 65 Gy respectively. We applied the criteria for acceptable femoral head doses set out in Report 62 from the International Commission on Radiation Units and Measurements (ICRU) [37] in which the volume that is covered by 52 Gy or more should be minimized (<5%). For each patient one 3-D CRT plan and one IMRT plan were produced to dosimetry. The Statistical Package for Social Sciences (SPSS) v. 19.0 was used for statistical analysis for all comparisons between two techniques. P value <0.05 was used to indicate statistical significance.

2.3 Pancreas tumor
Ten patients with pancreas tumor in supine position underwent CT planning, data was transferred to focal. Structures were manually contoured on the CT images to the target and critical organ (liver, spinal cord, and kidneys). Two plans were generated for each patient using 6 MV for both techniques, prescribed dose 45GY/25 fraction, treatment plans were optimized to ensure that 95% of the prescription dose was delivered at least to 95% of the PTV and, at the same time, with a maximum dose ≤110%. The dose distribution was calculated using the Superposition algorithm. The liver criteria no more than V33%, V50% and V66% of the liver volume should receive more than 50 Gy, 35 Gy and 30 Gy respectively. The mean dose for whole kidney (single) 15-18Gy and 30Gy to < 60% of one kidney, 15Gy to <50% of one kidney and the maximum dose for spinal cord was limited to 45Gy.

3. Results
The implementation of IMRT required extensive effort from the medical physicist because inverse planning systems normally require the user to define dose constraints for all targets and normal tissues (minimum, maximum, mean), numbers and orientations of beams, beam energy, and many dose optimization parameters allowed for the solution. The inverse planning system defines an objective function which describes how close the calculated solution is to the desired solution. This cost function is typically the sum of quadratic differences between calculated and prescribed doses for all points of interest within the patient. Optimization of a plan consists of modifying the weights of the beamlets and the power of each delineated organ until a minimum value of the cost function is achieved. To measure the quality of the IMP the results of each plan were compared with the 3DCP for the two treatment sites of this study and the final results showed that:

3.1. Prostate cases
3.1.1: Comparison for PTV
IMRT had better coverage (PTV95%) where (P = 0.0203) which considered significant. Median and Std. deviation (SD) (95.8±1.061, 94.7±1.324) for IMRT and 3DCRT respectively as showed in the figure 1. Homogeneity index values for IMRT vs 3D-CRT were (10±2.601, 8±2.215) respectively as showed in the figure 2. For the maximum doses in the PTV (PTV5%), median and Std deviation in PTV5% with IMRT plan were (105.65±1.360,) which was higher than conformal plan (103±1.11) but both results were in tolerance as showed in figure 3 and as indicated by P value (P=0.0002).

Figure 4 and 5 showed the dose-volume histograms (DVHs) for both plans for the same patient for PTV and organ at risk, these figures illustrated that dose for organ at risk with IMRT were lower than 3DCRT. Figure 6 showed the isodose curves for the 3DCRT and IMRT, respectively.

3.1.2: Comparisons for the OARs
The results showed that with Comparison of IMRT-plans with 3DCRT-plans in the same percentage of volume, the doses to the rectum and bladder irradiated for IMRT-plan were lower than that for 3DCRT-plan table1. Dose comparison for the different rectum volumes for IMRT and 3DCRT respectively were as followed

V15%, (69.85% vs. 95.50 %, P = 0.0001), V25%, (59% vs. 87.50 %, P<0.0001), V35% (50.50% vs. 78.40 % P= 0.0004), V50% (44% vs. 68.50%, P=0.0037), P values considered very significant.

Dose comparison for the different bladder volumes for IMRT and 3DCRT respectively were For, V15 %,( 78.70 % ±11.66 vs. 93.59%±11.66, P=0.0042), V25%, (61.50% ± 26.50 vs. 90%±19, P=0.0197), V35% (58%±27.18 vs. 76%±25.65, P=0.1368), and V50% (38.50 % ± 25.89 vs. 57± 30.77, P=0.1456)

For the femoral heads, very significant dose differences were found between IMRT-plan and 3DCRT-plan where dose received by V10% were 25.06% vs. 37.98% vs. 60.75%, P=0.0020 for right fumer and for left fumer 37.98% vs. 60.75%, P=0.0067), for IMRT and 3DCRT respectively.

3.2. Pancreas cases
The mean and standard deviation PTV coverage and homogeneity index for all cases are represented in figure 7, 8 and 9 .The difference was not significant, PTV98% in both techniques with IMRT (94.63±2.56) and conformal (94.74 ± 2.88).figure 10 and 11 showed dose volume...
histogram for PTV and OARs in comparison between 3DCRT and IMRT. Dose distributions of 3DCRT and IMRT in three CT slices of a patient with pancreas cancer represented in figure 12.

3.2.1. Dose to Critical Organs for Pancreas case.

3.2.1.1. Spinal Cord
As shown in figure 13, the value of the maximum dose to the spinal cord is significantly reduced with conformal (13.15±0.455) plan than IMRT (13.17±0.452). The spinal cord was irradiated to tolerance by two techniques, integral dose to cord with IMRT (0.26±0.18) higher than conformal plan (0.17±0.093), as shown in figure 14.

3.2.1.2. Liver
The mean and standard deviation (SD) values of V33%, V50% and V66% as shown in the figure 15, 16 and 17 were recovered by 29.87±16.88, 12.5±10.86 and 4.28±3.49 from the dose in the IMRT-plan and 28.89±17.97, 7.79±5.67 and 3.02 ± 1.72 in the 3DCRT-plan respectively.

The number of monitor higher with IMRT than 3D ,this indicate that the time of treatment longer than that of conformal in addition the time of plan and verification additional time that is necessary to move the gantry between different IMRT fields.

Discussion
This study analyzed two targets at different sites to compare sliding window IMRT and 3D conformal technique for patients with prostate and pancreatic cancers, aiming target coverage and an acceptable dose tolerance to the organs at risk. For prostate cancer our study showed both intensity modulated and 3D conformal techniques had a good PTV coverage and dose homogeneity figure 1. Homogeneity index (HI) showed higher value with IMRT than conformal figure 2. The main feature distinguishing IMRT from conformal radiotherapy is the ability to produce a concave dose distribution in the same time, minimize the rectal dose as much as possible achieved by introducing a posterior beam with gantry 180 degree. Intensity-modulated radiotherapy planning made significant reductions in all OARs when compared with 3DCRT (table 1). IMRT demonstrated a clear advantage of bladder sparing, dose differences considered significant between the IMRT and 3DCRT for V15%, V25%, V35% and V50% where the P values were P=0.0042, P=0.0197, P=0.1368 and P=0.1456 respectively, and recommend that bladder should be full to reduce the bladder dose. IMRT resulted in a significantly reduction for rectal dose V15%, V25%, V35% and V50% where the P values were P=0.0001, P<0.0001, P= 0.0004 and P=0.0037, which is highly significant. Volume 10% of femoral heads with IMRT plans was also highly significant dose differences were found between IMRT-plan and 3DCRT-plan, femoral heads were 25.06% vs 52.38% P=0.0020. IMRT plans showed that a larger volume of normal tissue was exposed to lower doses than with 3DCRT techniques (Howell R.M., Hertel N.E. et al., 2006, Kry S.F., Salehpour M. et al., 2005; and Mutic S., Low D.A. et al., 1998) and this radiobiological peculiarity has the effect of increasing the risk of a second malignancy (Followill D., Geis P., et al., 1997; and Kry S.F., Salehpour M. et al., 2005).

For patient with pancreatic cancer, our results indicate no significant differences were observed in PTV98% in both techniques where with IMRT the dose were (94.63±5.26) and for 3 DCRT (94.74± 2.88) figure 7. The homogeneity index was higher with IMRT than 3D-conformal figure 9. Three wedged beam arrangement [anterior and two opposed lateral ] performed with 3 D conformal plan, while five beams with IMRT plan, the number of monitor units were higher with IMRT than 3D conformal, this indicate that the time of treatment longer than that of conformal irradiation in addition to the time of plan and verification which add an additional time to the treatment time also there was a time that is taking to move the gantry between different IMRT fields (table 2). IMRT delivers a higher integral dose to the body because of leakage radiation resulting from the use of a greater number of fields and an increased number of monitor units, for patient with pancreatic cancer the doses

Conclusion
Our results showed superior PTV coverage and less OAR dose with IMRT plan comparing to 3D-CRT in prostate cases, IMRT technique enables significant increase in dose homogeneity in the PTV while allowing significant reduction in the doses received by the rectum, bladder and femoral head compared 3D-conformal.

In pancreatic cases the difference was not significant for PTV coverage and sparing OAR in both plans IMRT and 3 D conformal. It's better to use IMRT for prostate treatment to achieve good dose escalation but for the pancreatic patients it is not recommended to use the complicated IMRT technique.

Research Highlights
First of all a lot of times were spent to establish optimization procedures for IMRT. Secondly the effects of number of beams and beam orientations
on the plan optimization and it's impact on the patient irradiation doses were studied. Finally the dosimetric comparison between 3DCRT and IMRT were performed to define the cases which need a complex IMRT and that can be treated with the simple 3DCRT.

Authors’ Contribution and Competing Interests

The authors declare that they have no competing interests.

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