Dosimetric Study between Helical Tomotherapy, Rapidarc and Fixed Field Intensity Modulated Radiation Therapy for Pancreatic Cancer Cases

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Abstract

Objective: The aim of this present study was to investigate the potential clinical role of a novel treatment technique Rapid-Arc, Helical Tomotherapy (HT) and Conventional IMRT for post-operated pancreatic cancer. Material and Method: Five patients with post operated pancreatic cancer were selected for the dosimetric study. A convenient prescription (2Gy/fraction) was considered: 45 Gy for PTV and 55 Gy for SIBV according to RTOG protocol. For each patient three optimized plans were generated. Constraints to maximum and minimum dose to the PTV were also applied during dose optimization. Results: No statistical significance was observed between RA and HT independently from the MLC resolution meaning that for such small targets, although the resolution matters, the modulation capability of the optimization process is dominant. Concerning organs at risk, all techniques achieved largely the planning objectives described in the methods and proved to have the same degree of inter-patient variability.  

Keywords: Rapid Arc, Helical Tomotherapy, Intensity modulated radiotherapy

I. INTRODUCTION

The present study investigate the potential clinical role of a novel treatment technique Rapid-Arc, Helical Tomotherapy (HT) and Conventional IMRT for post-operated pancreatic cancer. Both helical tomotherapy and rapidarc (RA) are rotational radiotherapy modalities that use continuous gantry rotation with dynamic multileaf collimator (MLC). HT delivers intensity-modulated fan beams using binary MLC in a helical rotational pattern about the patient by translating the patient through rotational gantry (TomoTherapy Hi-Art II system) (1-3). Rapidarc, by contrast, uses a conventional linear accelerator (Linac) to deliver radiation in a cone beam geometry using dynamic MLC within one gantry rotation, with no couch translation during the treatment (4-6). The ‘conventional’ intensity modulation approach with fixed gantry and intensity modulated beams delivering the dose by means of the sliding window approach. The main drawback of IMRT are the more complex and time consuming treatment planning process and the need for more extensive physics quality assurance. In addition, IMRT uses a large number of static beams and monitor units (MUs) (5), which increase radiation delivery times up to 20min and also patient exposure to low –dose radiation.

In general, an increase in the number of IMRT beams increases the degree of freedom (6), making intensity modulation arc therapy a logical next step in IMRT delivery. Several optimization methods for arc therapy based on direct aperture optimization have been described (7-9). A recently described novel approach for volumetric modulated arc therapy enables IMRT like dose distributions to be delivered using a single rotation of the gantry (10).This concept has been clinically implemented in the Eclipse treatment planning software (Varian Medical Systems, Palo Alto, CA) under the name Rapid Arc (RA). In RA, the gantry speed, dynamic MLC movement and dose rate vary continuously during delivery. In addition, there is a full leaf interdigitation, allowing multiple small islands of dose to be delivered to the planning target volume (PTV) at each gantry position. Clinical introduction of such new treatment techniques should be preceded by detailed validation of a range of plans (11,12). Extensive studies on treatment planning or dosimetric validation and comparision of RA dose distribution with those obtained by existing IMRT techniques have not yet been reported.

Pioneered by Mackie et al.(1,2), HT was made commercially available by TomoTherapy Inc., and it has been used for a wide variety of applications in clinical radiation oncology(7-9). Each gantry rotation consists of 51 equally spaced beam projections and 64 binary MLC leaves in each projection. Each MLC leaf is individually controlled and allows intensity modulation within a full
range (0-100%) of each projection. Projection time is limited by the gantry rotation speed (15-60 sec). The degree of intensity modulation is determined by the modulation factor, which is the maximum leaf open time divided by the average leaf open time. Similar to helical computed tomotherapy (CT), the degree of fan-beam overlapping in HT is determined by the pitch factor, which is the ratio of couch translation per rotation to the jaw width. In the current released version (version 3.1.4) the jaw width options are 1.0, 2.5, and 5.0 cm.

Single arc refers that continuously delivers dose throughout one gantry rotation (6,15,16), as opposed to delivering several discrete intensity patterns with multiple gantry rotations. Dose distributions, comparable to a conventional IMRT technique, can be delivered to a conventional IMRT technique, can be delivered in 2 to 4 minutes. Several single arc products are commercially available for clinical implementation, such as Varian’s Rapidarc (RA) (Varian Medical System, Palo Alto, CA) adopted from the work of Otto (6). RA delivers radiation in a continuous gantry sweep with dynamic variation of MLC positions, dose rate and gantry speed. A RA MLC sequence consists of a series of aperture shapes and weights for the individual beam angles within the rotational arc. In single arc, only one aperture shape is assigned to each beam angle without intensity modulation in each aperture. The present study comparison was limited to two commercial solutions in addition to RapidArc. In the area of modulated arcs, we selected the Helical Tomotherapy (HT) approach, characterised as the RapidArc shown here, but for purely coplanar beam incidence. To benchmark results against consolidated solutions, we selected the rotational fan beam Helical tomotherapy approach.

The existing plan comparison studies were conducted by our institution. Therefore, the conclusions reached may be affected by that institution’s relative experience in the techniques of interests, in addition to patient case selection. A recent study has conducted a comparison and shown that rapidarc technique was able to provide shorter treatment time, with a reduction of approximately 40% and plan quality comparable to that of HT (22). The goal of the present study was to perform an unbiased comparison between HT and RA and conventional “fixed field” IMRT by eliminating the aforementioned shortcomings.

### II. METHODS AND MATERIALS

#### A. Patient Selection and Contouring

Five patients with post operated pancreatic cancer were selected for the dosimetric study (Table 1). These patients were randomly selected from the list of patients with pancreas cancer history. Anatomical data were acquired on computed tomography (CT) with adjacent slices 3 mm thick. All structures were contoured in Eclipse planning system (Version 8.6.14). All patients were prescribed doses to planning target volume (PTV) and simultaneously integrated boost volume (SIBV). The mean volume for PTV was 474.56 cm³, minimum 235.7 cm³ and maximum 700 cm³. The mean volume for SIBV was 213.11 cm³, minimum 76.73 cm³ and maximum 357 cm³.

#### B. Treatment Planning

A convenient prescription (2 Gy/fraction) was considered: 45 Gy for PTV and 55 Gy for SIBV according to RTOG protocol. Normalisation for all plans was set to the mean dose to the PTV and SIBV. For PTV the planning objectives were to cover at least 95% of the PTV with the 95% prescribed dose, minimum PTV dose > 90% prescribed dose and maximum dose < 107% prescribed dose. For OARs, the tolerance levels for maximum were spinal cord 45 Gy, for kidney’s mean dose, V20, for liver V30 < 66% normal liver volume, for duodenum maximum dose, V45, V50, V55 evaluated.

For each patient three optimized plans were generated. Constraints to maximum and minimum dose to the PTV were also applied during dose optimization. The goal of planning was to give the least possible amount of dose to all OARs while not exceeding these dose constraints or degrading tumour coverage. Plans were reviewed and accepted by our physician before being locked and swapped for analysis.

#### C. Helical Tomotherapy (HT) Plans

The HT planning software used for this study at our institute (Tata memorial hospital) was Hi-Art II version 3.1.4.32. The CT images were taken on GE 4DCT with slice thickness 3 mm. CT images were exported to the eclipse planning system for contouring the structures and planning purpose. The contoured CT structured set was exported to HT planning system for purpose of HT planning. The convolution-superposition algorithm based on the collapsed cone approach (23,24) was used for dose calculation in
HT planning system. Details on the HT optimisation process can be found in (3,13,14) and references therein. In this study, a jaw width of 2.5cm and a pitch factor of 0.3 were used for all the cases. The MLC is equipped with 64 leaves with a 0.625cm width at Isocentre. The modulation factor was set to be 2.5 for pancreas cases. A typical dose calculation grid (3.76X3.76X3 mm³) was used for all the cases. The HT machine commissioned for this planning study is calibrated to 880 cGy/min at a depth of 1.5 cm with 85 cm source-surface distance (SSD) setup.

D. Intensity Modulated Radiotherapy (IMRT) Plans

IMRT plans were optimized according to the ‘conventional’ intensity modulation approach with fixed gantry and intensity modulated beams delivering the dose by means of the sliding window approach. In Eclipse, the optimization engine of IMRT computes optimal fluence maps from dose volume constraints derived from the general planning objectives. Optimal fluence maps are then converted by a leaf motion calculator into actual fluence maps which are deliverable using a dynamic multileaf collimator according to the sliding window segmentation algorithm. Plans were individually optimized using five coplanar fields in axial plane. Optimizations and dose calculations were done with Eclipse version 8.6.14 (Varian medical systems). Beam geometry optimization was performed by means of the automatic tool implemented in Eclipse as part of the IMRT process. Plans were optimized using the High Definition MLC 120 (HD-MLC). This is characterized by a spatial resolution of 2.5mm at isocentre for the central 8cm and of 5mm in the outer 2x7 cm, a maximum leaf speed of 2.5cm/sec and a leaf transmission of 1%. Dose calculation was performed by means of the AAA algorithm with a spatial resolution of 2.5mm.

E. RapidArc (RA) Plans

At planning level, RapidArc consists of optimising a dose distribution from dose-volume objectives including the optimization from dose-volume objectives including the optimization of the main features of the linac head (e.g. head scatter) and of the MLC (e.g. speed, transmission, round leaf tip and tongue and groove design). To achieve the desired level of modulation required, the optimization is enabled to vary also the instantaneous dose rate from 0 to the maximum (600 or 1000 MU/min depending on the linac type), as well as the gantry rotational speed (from a maximum of 5.5°/s). To minimize the contribution of tongue and groove effect during the arc rotation and to benefit from the leaves trajectories non coplanar with respect to patient’s axis, the collimator rotation in RapidArc is set to values different from zero. In this study collimator was rotated to 45°. The entire gantry rotation is described in the optimisation process by a sequence of 177 control points (i.e. one control point (CP) every roughly 2°). A dedicated Progressive Resolution Optimisation (PRO) algorithm (Version 8.6.14) is used by RapidArc. With PRO the total 360° arc is initially represented by a small number of 10 control points (elementary beams) with a quite coarse resolution. During optimisation, the dose distribution is computed with a fast Multi-Resolution Dose Calculation Algorithm (MRDC). When dose is calculated for a particular control point, the MLC motion and dose rate are converted into a temporary fluence that models the linac head scattering, and the MLC leakage, rounded leaf ends, tongue and groove design as well as the leaf motion between neighbour control points. MRDC is based on the convolution superposition principle, and it used 3D convolution scatter computation. The PRO algorithm is highly interactive allowing users to adapt dose-volume constraints during the process as well as to go forward or backward in the multi resolution levels to speed up the process or to change optimisation strategy according to user’s philosophy. The final dose calculation is performed in Eclipse by means of the AAA algorithm (Version 8.6.14) only.

Plan comparison

The main focuses of our comparison between the three techniques were plan quality and treatment delivery efficiency. Upon the completion and final approval of all treatment plans, dose files of the HT plans were imported into Eclipse and compared with the RA plans. Although the dose calculation grid sizes were different, dose statistics reports of the three sets of plans were generated using the same sampling resolution and the same treatment planning systems. For the ease of comparison, all HT, RA and Fixed field IMRT plans were normalized such that 95% of the target volume received 100% of the prescription dose. Target dose coverage was evaluated by Homogeneity index was defined by Wu et al. (25):

$$HI = \frac{(D_2 - D_88) \times 100}{D_p}$$

Where $D_2$ and $D_{88}$ represent the doses to 2% and 98% of the PTV; $D_p$ represent the prescription dose. Equation indicates that lower homogeneity values indicate a more homogeneous target dose. Analysis was performed on Dose-Volume Histograms (DVHs) computing several standards (15,16) parameters. The confirmity index described by Feuvret et al. (26) and van’t Riet et al. (27) is used to assess the target confirmity. It is defined as the product of the percentage of PTV encompassed by the 95% isodose volume, and the proportion of the 95% isodose volume accounted for by the PTV:

$$CI = \frac{(PTV \text{ encompassed by the } 95\% \text{ isodose/PTV}) \times \left( \frac{\text{PTV encompassed by the } 95\% \text{ isodose}}{95\% \text{ isodose volume}} \right)}{95\% \text{ isodose volume}}$$

The CI ranges from 0 to 1, where 1 is the ideal value.
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Fig. 3: (DVH)

Fig. 2: (30 and 60 % isodose)
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III. RESULTS

In fig 1, 95 % isodose distributions of prescribed dose to PTV and SIBV on axial, coronal and saggital views are presented for all the techniques for a pancreas cancer cases to provide qualitative overview. In fig 2, shows two low-medium isodose (30% and 60%) to illustrate the differences present in healthy tissue irradiation among the techniques. Fig 3 shows, for PTV, SIBV and most involved OARs, respectively, the cumulative DVHs averaged over all the patients. Tables 2 summarise quantitative analysis of PTV, SIBV and OARs data.

Table - 2

An overview of all investigated DVH-parameters as mean values ± standard deviation (SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Helical</th>
<th>RapidArc</th>
<th>IMRT</th>
<th>t-Test: Paired Two Sample for Means (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tomotherapy</td>
<td></td>
<td>HT vs RapidArc</td>
<td>HT vs IMRT</td>
</tr>
<tr>
<td>MU</td>
<td>2129 ± 662</td>
<td>469 ± 27</td>
<td>1150 ± 223</td>
<td>0.0051</td>
</tr>
<tr>
<td>Treatment Time (min)</td>
<td>2.45 ± 0.76</td>
<td>1.17 ± 0.07</td>
<td>2.87 ± 0.56</td>
<td>0.0210</td>
</tr>
<tr>
<td>Left Kidney V20 %</td>
<td>0.32 ± 0.44</td>
<td>11.95 ± 10.75</td>
<td>10.21 ± 9.77</td>
<td>0.0660</td>
</tr>
<tr>
<td>mean Dose (Gy)</td>
<td>8.74 ± 1.18</td>
<td>13.70 ± 3.52</td>
<td>11.97 ± 2.46</td>
<td>0.0143</td>
</tr>
<tr>
<td>Right Kidney V20 %</td>
<td>19.78 ± 17.7</td>
<td>51.63 ± 14.08</td>
<td>21.62 ± 19.11</td>
<td>0.0091</td>
</tr>
<tr>
<td>mean Dose (Gy)</td>
<td>15.21 ± 4.14</td>
<td>19.67 ± 3.70</td>
<td>14.4 ± 3.79</td>
<td>0.0324</td>
</tr>
<tr>
<td>Liver V30 %</td>
<td>13.18 ± 10.59</td>
<td>9.44 ± 7.95</td>
<td>11.01 ± 7.74</td>
<td>0.0594</td>
</tr>
<tr>
<td>Liver V40 %</td>
<td>6.54 ± 5.68</td>
<td>5.02 ± 4.49</td>
<td>5.14 ± 4.53</td>
<td>0.1703</td>
</tr>
<tr>
<td>Spinal Cord Maximum Dose (Gy)</td>
<td>21.10 ± 4.91</td>
<td>21.32 ± 8.57</td>
<td>32.86 ± 7.64</td>
<td>0.9790</td>
</tr>
<tr>
<td>Duodenum max Dose (Gy)</td>
<td>60.43 ± 0.43</td>
<td>60.34 ± 1.06</td>
<td>54.84 ± 4.32</td>
<td>0.9220</td>
</tr>
<tr>
<td>Duodenum V45 %</td>
<td>69.02 ± 24.72</td>
<td>69.44 ± 26.35</td>
<td>64.05 ± 28.32</td>
<td>0.8058</td>
</tr>
<tr>
<td>Duodenum V50 %</td>
<td>51.65 ± 30.26</td>
<td>58.47 ± 29.87</td>
<td>45.7 ± 31.42</td>
<td>0.1570</td>
</tr>
<tr>
<td>Duodenum V55 %</td>
<td>37.10 ± 32.19</td>
<td>42.23 ± 32.22</td>
<td>24.22 ± 25.95</td>
<td>0.1061</td>
</tr>
<tr>
<td>PTV max Dose (Gy)</td>
<td>60.84 ± 0.44</td>
<td>60.84 ± 0.96</td>
<td>57.53 ± 0.35</td>
<td>0.9952</td>
</tr>
<tr>
<td>PTV mean Dose (Gy)</td>
<td>53.97 ± 0.97</td>
<td>54.51 ± 0.79</td>
<td>51.48 ± 0.42</td>
<td>0.2358</td>
</tr>
<tr>
<td>PTV D2 (Gy)</td>
<td>59.86 ± 0.50</td>
<td>59.46 ± 0.84</td>
<td>56.43 ± 0.37</td>
<td>0.4223</td>
</tr>
<tr>
<td>PTV D98 (Gy)</td>
<td>44.68 ± 0.17</td>
<td>44.71 ± 1.63</td>
<td>43.46 ± 0.65</td>
<td>0.9684</td>
</tr>
<tr>
<td>Total Volume (cc)</td>
<td>470.95 ± 179.46</td>
<td>474.5 ± 180.65</td>
<td>474.56 ± 180.71</td>
<td>0.0043</td>
</tr>
<tr>
<td>HI</td>
<td>0.34 ± 0.01</td>
<td>0.33 ± 0.05</td>
<td>0.29 ± 0.02</td>
<td>0.7005</td>
</tr>
<tr>
<td>CI95%</td>
<td>1.00 ± 0.00</td>
<td>0.63 ± 0.09</td>
<td>0.45 ± 0.06</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

Fig. 1: (95 % isodose)
For PTV and SIBV, it can be seen from both average DVH graph and summary of numerical findings that all techniques provided good and equivalent results although statistically significant differences can be observed between the various couples from t-paired tests (p-value). The most relevant findings are linked to the superior coverage of HT and able to save the left kidney better than with the other techniques due to directional blocking. In terms of inter-patient dose variability, expressed by the standard deviation computed per each technique, all approaches are comparable. No statistical significance was observed between RA and HT independently from the MLC resolution meaning that for such small targets, although the resolution matters, the modulation capability of the optimization process is dominant.

Concerning organs at risk, all techniques achieved largely the planning objectives described in the methods and proved to have the same degree of inter-patient variability. The statistical significant differences revealed by paired t-paired tests should therefore be considered anymore subject to valuable costs in the optimisation process. With this disclaim enforced, it shall be noticed that with conventional fixed field IMRT, we are able to achieve better or comparable sparing for the Right kidney and duodenum compared with Rapid Arc by selecting beam angles that restricts the beam. Liver dose was comparable in all the three techniques. Relatively to the normal pancreas and the total healthy tissue (body volume in the CT dataset minus the target), RA plans improved HT findings independently from MLC resolution while, systematically, the plans based on High definition MLC resulted better results. The integral dose analysis showed that IMRT has the minimum impact while, among rotational techniques, the RA is potentially superior to HT (significantly for RA_HD120) and that finer MLC resolution can enhance the effect.

The number of monitor units and treatment time for all three techniques (RA, HT and IMRT) plans were noted in Table 2. Averaging over the 5 plans studied, the MU with HT were 4.5 times more compared to RA and 1.85 times more compared to IMRT. When comparing the treatment time, RA had an average beam on time of 1.17 minutes (range, 1.09 -3.53 minutes) and 2.45 times shorter than that for IMRT (range, 2.19-3.53 minutes).

### IV. DISCUSSIONS

Our study showed that the optimal choice of radiation therapy modality for safe dose escalation depends on the pancreatic tumor position in relation to OAR anatomy. Rapidarc, Helical tomotherapy, IMRT and 3DCRT plans showed advantageous results, but for different tumor positions. 3DCRT plans presented considerably inferior target coverage compared with the other three modalities. Due to PTV, SIBV and OAR overlap, full target coverage was not met by any technique or tumor position for plans that fully respected OAR constraints with the best coverage achievable. However, interesting conclusions can be drawn from the plans generated with full target coverage which can be extrapolated to new cases.

This study reports a comparison of the helical tomotherapy (HT) technique compared to RapidArc, fixed beam IMRT. Similar investigations on different indications are appearing. Palma et al. investigated RapidArc progenitor on prostate showing that variable dose rate volumetric arc modulation is beneficial compared to IMRT or constant dose rate [29]. Fogliata et al. investigated RapidArc on small benign brain tumors compared to IMRT and helical tomotherapy [16]. It is expected that in a relatively short time-frame a systematic insight of the clinical role of the novel volumetric modulated arc therapy approaches will appear. The planning case selected for this investigation was the cancer of pancreatic since it is a demanding indication.

As all comparative studies, also the present one is potentially affected by limitations that shall be clarified. The most important are linked to the difficulty to eliminate any type of bias in the elaboration of dose plans induced different calculation algorithm. The dose calculation algorithm and all tools to generate dose distributions, DVH and analysis are the same for all plans. Compared to IMRT, which has been proven to be superior to conventional treatments [17,20,27,30,34,41], RapidArc and helical tomotherapy allows one to keep the same PTV and SIBV coverage with an improved homogeneity and better conformity and, at the same time, presented a major reduction of irradiation of kidney, liver and spinal cord over the entire medium to high dose levels with highly statistically significant differences.

RapidArc allowed a strong reduction of MU/Gy compared to IMRT (roughly a factor 2) and helical tomotherapy. It is known and accepted that, in treatments with linear accelerators, the scattered radiation impinging on the patient’s body outside the treated volume is at first-order directly proportional to the monitor units applied (lucca cozzy paper ref).

One of the objectives of RapidArc is the capability to deliver treatments in short times. For the cases under investigation, beam-on time was estimated to be less than 1.5 min. Studies from other IMAT approaches [12,13] reported mean delivery time of 6.3
min for medium size tumors increasing to about 14 min for large volumes. Helical Tomotherapy [4] reported average beam-on time of 11 min.

V. CONCLUSION

Our study showed that the optimal choice of radiation therapy modality for safe dose escalation depends on the pancreatic tumor positions relative to OAR anatomy. IMRT allows more conformal dose distribution in the high-dose regions, whereas PT reduces low doses to GI-OAR. This GI-OAR sparing gain with PT is an interesting aspect for further clinical investigation in combination with future attempts of systemic treatment intensification.

REFERENCES