WHOLE ABDOMINOPELVIC RADIOTHERAPY (WAPRT) USING INTENSITY-MODULATED ARC THERAPY (IMAT): FIRST CLINICAL EXPERIENCE

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Purpose: Whole abdominopelvic radiation therapy (WAPRT) is a treatment option in the palliation of patients with relapsed ovarian cancer. With conventional techniques, kidneys and liver are the dose- and homogeneity-limiting organs. We developed a planning strategy for intensity-modulated arc therapy (IMAT) and report on the treatment plans of the first 5 treated patients.

Methods and Materials: Five consecutive patients with histologically proven relapsed ovarian cancer were sent to our department for WAPRT. The target volumes and organs at risk (OAR) were delineated on 0.5-cm-thick CT slices. The clinical target volume (CTV) was defined as the total peritoneal cavity. CTV and kidneys were expanded with 0.5 cm. In a preset range of 8° interspaced gantry angles, machine states were generated with an anatomy-based segmentation tool. Machine states of the same class were stratified in arcs. The optimization of IMAT was done in several steps, using a biophysical objective function. These steps included weight optimization of machine states, leaf position optimization adapted to meet the maximal leaf speed constraint, and planner-interactive optimization of the start and stop angles. The final control points (machine states plus associated cumulative monitor unit counts) were calculated using a collapsed cone convolution/superposition algorithm. For comparison, two conventional plans (CONV) were made, one with two fields (CONV2), and one with four fields (CONV4). In these CONV plans, dose to the kidneys was limited by cerrobend blocks. The IMAT and the CONV plans were normalized to a median dose of 33 Gy to the planning target volume (PTV). Monomer/polymer gel dosimetry was used to assess the dosimetric accuracy of the IMAT planning and delivery method.

Results: The median volume of the PTV was 8306 cc. The mean treatment delivery time over 4 patients was 13.8 min. A mean of 444 monitor units was needed for a fraction dose of 150 cGy. The fraction of the PTV volume receiving more than 90% of the prescribed dose (V90) was 9% higher for the IMAT plan than for the CONV4 plan (89.9% vs. 82.5%). Outside a build-up region of 0.8 cm and 1 cm away from both kidneys, the inhomogeneity in the PTV was 15.1% for the IMAT plans and 24.9% for the CONV4 plans (for CONV2 plans, this was 34.9%). The median dose to the kidneys in the IMAT plans was lower for all patients. The 95th percentile dose for the kidneys was significantly higher for the IMAT plans than for the CONV4 and CONV2 plans (28.2 Gy vs. 22.2 Gy and 22.6 Gy for left kidney, respectively). No relevant differences were found for liver. The gel-measured dose was within clinical planning constraints.

Conclusion: IMAT was shown to be deliverable in an acceptable time slot and to produce dose distributions that are more homogeneous than those obtained with a CONV plan, with at least equal sparing of the OARs.

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Intensity-modulated arc therapy (IMAT), Whole abdominopelvic radiotherapy (WAPRT), Ovarian cancer.

INTRODUCTION

The treatment options for most patients with relapsed ovarian cancer are palliative. For patients who relapse within 12 months after platinum-based schedules, second- or third-line chemotherapy is often used, but the response rates average between 10% and 30% (1).

A difficult problem to palliate is bowel obstruction. Surgery may be attempted but the disease is often multifocal making palliative resection impossible. In reports of
Redman et al. (2) and Krebs et al. (3), 10–15% of patients died within 8 weeks after surgery and 35–38% had no clinical benefit. The results of chemotherapy for bowel obstruction are disappointing. In a report by Abu-Rustum et al. (4), a response was observed in only 1 of 18 patients treated with chemotherapy for bowel obstruction. Radiation therapy seems to compare favorably with second- or third-line chemotherapy, with symptom response rates between 63% and 79% with a median duration between 4 and 9 months (5–7). Given the pattern of spread of ovarian cancer, whole abdominopelvic radiation therapy (WAPRT) could be the radiation technique of choice, eventually with a boost to sites of gross tumor.

Maximum tolerated dose levels to the whole kidney are often set to 20 Gy or less. When the kidneys are blocked from radiation, conventional techniques result in underdos- age of the peritoneal regions in the blocked areas.

We investigated the potential of intensity-modulated radiation therapy (IMRT) to spare kidneys and liver. For reasons described in the discussion section, we selected intensity-modulated arc therapy (IMAT) (8) as the most appropriate IMRT technique for WAPRT.

This article describes the results of the translational research that was performed to bring IMAT into the clinic for WAPRT. We report on treatment planning and delivery for the first 5 patients treated with IMAT-WAPRT. The clinical results of the Phase I study will be reported elsewhere.

METHODS AND MATERIALS

Delineation of target volumes and OARs

Between November 2001 and October 2002, 5 patients with a relapse of a histologically proven adenocarcinoma of the ovary were treated by IMAT. All patients signed informed consent for IMAT to the whole abdomen. A planning computed tomography (CT) scan was performed with the patient lying supine, with both arms resting under the head. The upper border of the scanned volume was located 10 cm cranial to the diaphragm, whereas the lower border was defined as 10 cm caudal to the obturator foramina. Several 0.5-cm-thick sequential CT slices were acquired without contrast enhancement. Clinical target volume (CTV) was defined as the total peritoneal cavity, with the inclusion of iliac and para-aortic lymph node regions. A 0.5-cm rim of liver, adjacent to the peritoneum, was also included into the CTV. The upper CTV boundary was defined by the highest CT slice on which the diaphragmatic dome was visible, and the most caudal drawing of the CTV was on the level of the bottom of the obturator foramina. A planning target volume (PTV) was made by a 3D expansion of the CTV with a margin of 0.5 cm in all directions. The kidneys and the liver (hereafter called OARs: organs at risk) were drawn as visualized on CT, and the kidneys were expanded with 5 mm (kidney_exp_5mm), to account for setup inaccuracy and organ motion. PTV and OARs overlap, which would result in a conflicting requirement from the optimization algorithm. A similar problem arises with those parts of the PTV in the build-up region. Both problems were solved by defining subvolumes inside the PTV that are used as optimization volumes (PTV_optim). PTV_optim was nowhere closer than 0.8 cm to the skin surface or 0.5 cm to the expanded kidneys. A surrounding structure was made by subtracting the PTV from the total scanned volume of the patient. This structure (sur_0cm) was used to avoid hot spots outside the PTV. A general description of the use of PTV subvolumes and surrounding structures for IMRT plan optimization is found elsewhere (9).

IMAT planning procedure

Generation of machine states by ABST. An anatomy-based segmentation tool (ABST) was developed at our institution to create segments for step-and-shoot IMRT (10). For IMAT planning, ABST is used to create an initial set of segments, which we call machine states. A machine state is described by a set of machine parameters that uniquely define the beam incidence, aperture, and photon beam quality. After definition of the isocenter location and with the collimator, table top and isocenter rotations at 0°, ABST generated machine states per 8° of gantry rotation. Restriction of the range of gantry angles was needed to avoid beams traversing metal components of the couch before entering the patient. The couch on the linear accelerator (Elekta, Crawley, UK) used for the IMAT treatments has two C-arms, which can be positioned at one of the 30° discrete angles. The largest range of possible gantry angles was obtained by setting the arms at 120°, measured from their lateral position (Fig. 1). For Patients 2, 3, and 5, a class solution was used, implying that the initial machine states were generated using a fixed set of parameters, including start-and-stop gantry angles, widths of the segments, and conformal avoidance structure. The arcs used by the class solution are shown in Fig. 1. For Patient 4, where the craniocaudal extent of the PTV was 42 cm, a second isocenter was defined 12 cm from the first isocenter in caudal direction. Only a longitudinal table shift is required to perform the transition between the two isocenters. An additional “pelvic arc” was made around a structure called PTV_pelvis, with the L5-S1 intervertebral space as the upper border. The collimator was rotated by 90° to have the leaf movements in the craniocaudal direction and allow for feathering in the junction region (11).

For each gantry angle, ABST generates multiple machine states that differ only by apertures of the multileaf collimator (MLC). Each beam’s-eye view (BEV) projection of a MLC aperture covers a part of the PTV at one side of the anatomic structure that is to be avoided. A margin of 0.8 cm around the PTV is used to account for penumbra. For each gantry angle, the machine states differ from each other by the degree of coverage of the BEV projection of the PTV. For a detailed description of ABST, refer to De Gersem et al. (10). These machine states are useful to create intensity levels that increase with decreasing distance to the anatomic structure that is to be spared. It was shown by Brahme and others (12, 13) that such intensity profiles are useful to
create homogeneous dose distributions to a concave PTV that conformally avoid anatomic structures at risk. The machine states were stratified in classes, the first class consisting of machine states with the largest area of MLC aperture, the second class consisting of machine states with the second largest area of MLC aperture, and so on. Because of the algorithm inside ABST that creates MLC apertures avoiding anatomic structures with—in this case—smooth surfaces, MLC apertures, which belong to the same class of machine states, do not differ much from one gantry angle to the next, their angular separation being only $8^\circ$. Hence, the leaf travel required when moving from one gantry angle to the next is small for machine states of the same class, which is preferable for dynamic transitions as in IMAT.

For Patients 2–5, an additional posterior “sliding window” intensity-modulated beam with a $90^\circ$ collimator rotation was used. For this beam, the table bars were put on their most lateral position. Because of the position of these metal bars, and the impossibility to prescribe arcs traveling over the $180^\circ$ gantry point, the range for posterior arcs is very limited. Therefore, a sliding window intensity-modulated beam with static gantry angle was preferred to boost the most posterior region of the PTV. The control points for this sliding window were made manually. For Patient 4, the most caudal isocenter was selected for this sliding window beam.

**Creation and optimization of control points.** The machine instruction file to deliver arc therapy with dynamic MLC consists of a sequence of control points (see Fig. 1). A control point is defined as a machine state plus a monitor unit count (MUC) value. Delivery of a sequence of control points implies that the prescribed machine state has to be

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**Fig. 1.** Class solution for the IMAT plan. A transverse plane through the patient can be appreciated, with the PTV, the left kidney (LK) and the right kidney (RK). The arcs are depicted by circle segments. Machine states for one arc (S0R LK) are shown every $16^\circ$, from $-128^\circ$ to $0^\circ$. The thick gray lines represent the jaw position, each small white bar stands for one leaf. **Abbreviations:** S0R LK: Arc composed by the machine states covering the total BEV projection of the PTV passing the right side of the LK. S0L RK: Arc composed by the machine states covering the total BEV projection of the PTV passing the left side of the RK. S1R LK: Arc composed by the machine states covering a $3 \text{ cm}$ wide area of the PTV at the right side of the LK. S1L RK: Arc composed by the machine states covering a $3 \text{ cm}$ wide area of the PTV at the left side of the RK. The metal C-arms are shown as the gray squares, respectively in their most lateral position (asterisk) for the sliding window, and in their $120^\circ$ position (+ sign). The large dashed arrow represents the beam direction for the delivery of the sliding window (SW).
reached at the MUC value for each control point. The transition from a control point to the next is slaved by the monitor unit (MU) counter; each parameter (leaf positions, jaw positions, and gantry angle) that changes between two control points is linearly interpolated as function of the MUC value. The beam is paused if the control software detects that a machine parameter is outside tolerance to the (linearly interpolated) position prescribed by the machine state. Control point optimization involves the machine states—and more precisely, the leaf positions—as well as the MUC values and is done by a segment outline and weight adapting tool (SOWAT) (14), modified for IMAT purposes (SOWAT-IMAT). The main difference between SOWAT and SOWAT-IMAT resides in the maximal leaf velocity (MLS) constraints. After the control point generation and after each leaf position optimization cycle, a leaf velocity constrainer (LVC) adapts leaf positions of all control points to obey maximum leaf speeds, minimum distances to opposed and diagonally opposed leaves, and maximum leaf position extends (method unpublished). MUCs are optimized for each step, a step being defined as the transition from one control point to the next. The objective function on which the optimization is done is a biophysical model and has been described and discussed elsewhere (15, 16).

Transformation to deliverable arcs. As a result of SOWAT-IMAT, n machine states and n-1 weights are obtained. These weights are numbers of monitor units that have to be delivered while the machine moves from one control point to the next. Apart from leaf and jaw travel, such motion involves a 8° gantry rotation. Because the Elekta SL-series of linear accelerators was designed to deliver arcs with a gantry rotation speed directly proportional to the dose rate, the number of monitor units delivered per degree (angular delivery rate) must remain constant over the whole arc. This condition is not secured by SOWAT-IMAT. In fact, the (requested) angular delivery rate may be different for each 8°-sector of gantry rotation. This problem is solved by splitting each arc, which features a variable angular delivery rate into multiple overlapping arcs each with a constant angular delivery rate (Fig. 2). This procedure also provides the start-and-stop angles of the delivered arcs. The plan is finalized by a SOWAT-IMAT optimization cycle, which involves optimization of leaf positions and the angular delivery rate (equal for all sectors of the arc to keep the angular delivery rate constant within each arc).

Dose prescription and computation. The prescribed dose was 33 Gy (median dose in the PTV), given in 22 fractions. Except for the first patient, IMAT plans were accepted using the following clinical criteria: less than 5% of the PTV volume was allowed to receive more than 107% of the prescribed dose, and more than 95% of the volume of PTV_optim had to receive more than 90% of the prescribed dose; less than 5% and 20% of the kidneys_exp_5mm should receive more than 30 Gy and 25 Gy, respectively, whereas the median dose had to be lower than 18 Gy; the median liver dose was constrained to 30 Gy. After clinical

Fig. 2. Picture representing the angular delivery rate. One “virtual” arc (dashed line) as well as three deliverable arcs (solid lines) are shown. The “virtual” arc is not deliverable on the Elekta linac. The deliverable arcs approximate the optimized virtual arc. The final angular delivery rate (W) of the deliverable arcs is optimized as described in the text.

Fig. 3. Adapted Rando phantom as used for the gel dosimetry. At each side of the Barex cast, three Rando slices were added to obtain full scatter conditions. Tape is attached to the phantom to draw laser lines in transverse, sagittal, and coronal reference planes. Seven markers are attached to the phantom on the laser lines to facilitate positioning. The transverse plane indicated in the middle of the barex phantom is 13.5 cm cranial to the treatment isocenter. A barex screw is used to close the phantom at the place where the gel was inserted, visible left to the sagittal plane.
IMAT for whole abdominopelvic radiotherapy ● W. DUTHOY et al.

Table 1. Details about the intensity-modulated arc therapy treatments

<table>
<thead>
<tr>
<th>Isocenters</th>
<th>Arcs</th>
<th>Control points</th>
<th>Monitor units</th>
<th>Delivery time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>1</td>
<td>11</td>
<td>73</td>
<td>568</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1</td>
<td>7 + 1 SW</td>
<td>110</td>
<td>387</td>
</tr>
<tr>
<td>Patient 3</td>
<td>1</td>
<td>7 + 1 SW</td>
<td>78</td>
<td>378</td>
</tr>
<tr>
<td>Patient 4</td>
<td>2</td>
<td>7 + 1 SW</td>
<td>99</td>
<td>528</td>
</tr>
<tr>
<td>Patient 5</td>
<td>1</td>
<td>6 + 1 SW</td>
<td>148</td>
<td>359</td>
</tr>
</tbody>
</table>

Abbreviation: SW = sliding window.
For the first patient, no systematic measurements were done concerning the delivery time. The monitor units are for one fraction of 150 cGy.

Constraints were met by the optimization procedure, a final dose computation was performed for 18 MV with the collapsed cone convolution/superposition algorithm from Pinnacle (Philips Medical Systems, Best, The Netherlands). A final optimization of the MUs of all arcs was done using the results of this dose computation. The value of a MU is such that 100 MUs correspond to 1 Gy at reference depth (5 cm for 6 MV and 10 cm for 18 MV) for a 10 × 10 cm field and a source-detector distance of 100 cm.

**IMAT treatment delivery.** For each arc, a prescription file containing the sequence of control points and related monitor units is generated and networked to an SLiPlus 18-MV linear accelerator (Elekta). The IMAT treatment is delivered in local service mode using prototype dynamic control software (Elekta), operating as described previously (17). Delivery of dynamic prescriptions is not possible in clinical mode on the Elekta linear accelerators. The local service mode is operated in the same interlock class as in clinical mode. Therefore, tolerances used by the linac’s control system are the same as for clinical mode.

**Conventional plans**

For each patient, two different conventional (CONV) plans were made. The first plan was the widely used “AP/PA” technique, using an anterior and a posterior field (CONV2). A second plan used four beams (CONV4): anterior, posterior, and two lateral fields. The field margins were drawn with a 1-cm margin around the PTV in all directions. Kidney blocks covered the BEV projection of the kidneys with a margin of 0.5 cm. For the CONV2 plans, the posterior field was duplicated in two segments, an open segment and a segment where kidney blocks were inserted. Respectively, 6-MV and 18-MV photons were used for the anterior and posterior field. For the CONV4 plans, all four fields were duplicated in two segments each, an open segment and a segment with kidney blocks. Here, 18-MV photons were used for all fields.

Optimization of the relative segment weights was done by the planner to reach a median dose to the expanded kidneys between 18 and 20 Gy. Median dose to the liver was constrained to 30 Gy. Dose computation was done with the same collapsed cone convolution/superposition algorithm.

**Treatment evaluation**

Delivery time, defined as the time between the start of the first arc and the end of the last arc or sliding window, was measured for Patients 2–5. Additionally, the setup time was measured from the entrance of the treatment room by the patient to the start of the first arc. This includes the time necessary to acquire portal images and correction of the patient position.

Comparison of dose distributions obtained with the CONV2, CONV4, and the IMAT plan was done after normalizing the median dose of the PTV to 33 Gy. To evaluate the dose homogeneity in the target volumes, an inhomogeneity factor U_{95/5} was defined as the difference between the 95th percentile dose (D_{95}) and the 5th percentile dose (D_{5}), divided by the median dose (D_{med}). We preferred to use the D_{95} and the D_{3} above the maximum and minimum dose, because an underdosage was allowed in the region close to the kidneys. Other endpoints for the target volumes were the first percentile dose (as a surrogate for minimum dose), the 99th percentile dose, and the ratio of volume of the target structure receiving more than 95% of the prescribed dose (V_{95}) over the total volume. For the parallel-element organs kidney and liver, the D_{med} was used. The dose–volume histograms (DVHs) were reconstructed for the 5 patients by calculating the mean dose and the standard error of the mean at every 5% volume level. The paired Student t test was used. All tests were two-tailed and p < 0.05 was considered as statistically significant.

**Dosimetric verification of the IMAT treatment**

Monomer/polymer gel dosimetry was used for 3D dose verification of the whole IMAT procedure. A deoxygenated hydrogel infused with acrylic monomers forms the basis for this dosimetric technique (18). Highly reactive radicals, formed by radiolysis during irradiation of the gel, initiate a polymerization reaction. The amount of polymer formed is related to the absorbed dose. Formation of polymer clusters in the water-equivalent gel increases the local spin-spin relaxation rate (R2), a typical magnetic resonance (MR) contrast parameter. Therefore, MR imaging (MRI) can be used to visualize the amount of polymer formed and subsequently the dose distribution in the gel. With monomer/polymer gel dosimetry, it is possible to obtain absorbed dose information in 3D with high spatial accuracy (19). For a
Fig. 4. (a) Intensity profiles (rescaled) for the delivered plan of Patient 2. The CT slice through the isocentric plane is shown, with the dose distribution in Gy. The PTV (dotted line) extends outside the scanned volume (asterisks). (a) Intensity profiles, generated at a range of gantry angles from $-128^\circ$ to $128^\circ$, are plotted around the CT slice. (b) Intensity profiles for the gantry at $-104^\circ$, $104^\circ$ and for the posterior beam, delivered as a sliding window ($180^\circ$).
more detailed review on this subject, the reader is referred to De Deene et al. (20).

A Barex (Cifra, Chateau Thierry, France) cast was vacuum molded on the abdominal region of the Rando phantom (Alderson Research Laboratories, Stamford, CT). At our laboratory, the maximum amount of monomer/polymer gel that can be produced in one batch is 10 L. Hence, the entire volume irradiated with IMAT can not be verified by one gel dosimetry experiment. We chose to limit the phantom geometry to that part of RANDO containing the (dosimetrically most interesting) region around the kidneys. Supports on the cranial and caudal side, marker lines and placement of markers (Medtronic, Louisville, KY) on the surface facilitated a reproducible positioning of the gel phantom during CT scanning, IMAT delivery, and MRI (Fig. 3). Three supplemental Rando slices were placed alongside the phantom on the cranial and caudal side during CT scanning, IMAT delivery, and MRI (Fig. 3). Supports on the cranial and caudal side, marker lines and placement of markers (Medtronic, Louisville, KY) on the surface facilitated a reproducible positioning of the gel phantom during CT scanning, IMAT delivery, and MRI (Fig. 3).

Table 2. Summary of the DVH data showing averages ± standard deviations

<table>
<thead>
<tr>
<th></th>
<th>IMAT</th>
<th>CONV2</th>
<th>CONV4</th>
<th>p value</th>
<th>p value</th>
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<tbody>
<tr>
<td>PTV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V_{95} (%)</td>
<td>82.2 ± 6.5</td>
<td>76.8 ± 5.2</td>
<td>0.11</td>
<td>73.6 ± 5.9</td>
<td>0.01</td>
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<tr>
<td>V_{90} (%)</td>
<td>89.9 ± 5.7</td>
<td>80.1 ± 4.6</td>
<td>0.01</td>
<td>82.5 ± 6.1</td>
<td>0.01</td>
</tr>
<tr>
<td>V_{107} (%)</td>
<td>2.7 ± 3.4</td>
<td>6.4 ± 3.3</td>
<td>0.18</td>
<td>7.2 ± 4.4</td>
<td>0.05</td>
</tr>
<tr>
<td>D_{1} (Gy)</td>
<td>19.0 ± 10.8</td>
<td>16.4 ± 9.1</td>
<td>0.09</td>
<td>16.5 ± 9.3</td>
<td>0.10</td>
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<tr>
<td>D_{90} (Gy)</td>
<td>35.8 ± 0.9</td>
<td>36.1 ± 0.6</td>
<td>0.53</td>
<td>36.5 ± 0.9</td>
<td>0.02</td>
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<tr>
<td>U_{95/5} (%)</td>
<td>28.1 ± 15.8</td>
<td>42.3 ± 7.9</td>
<td>0.03</td>
<td>34.4 ± 10.9</td>
<td>0.10</td>
</tr>
<tr>
<td>PTV_\text{optim}</td>
<td></td>
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<tr>
<td>D_{1} (Gy)</td>
<td>27.0 ± 2.8</td>
<td>21.7 ± 0.9</td>
<td>0.02</td>
<td>24.5 ± 1.2</td>
<td>0.12</td>
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<td>U_{\text{5/5}} (%)</td>
<td>15.1 ± 5.8</td>
<td>34.9 ± 2.5</td>
<td>$&lt;$0.01</td>
<td>24.9 ± 4.1</td>
<td>0.01</td>
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<tr>
<td>Left kidney (expanded)</td>
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<tr>
<td>D_{\text{med}} (Gy)</td>
<td>16.1 ± 3.6</td>
<td>19.9 ± 0.6</td>
<td>0.11</td>
<td>19.4 ± 0.4</td>
<td>0.11</td>
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<tr>
<td>D_{95} (Gy)</td>
<td>28.2 ± 1.3</td>
<td>22.6 ± 0.8</td>
<td>$&lt;$0.01</td>
<td>22.2 ± 0.4</td>
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<td>Right kidney (expanded)</td>
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<td>D_{\text{med}} (Gy)</td>
<td>13.6 ± 3.9</td>
<td>19.3 ± 1.5</td>
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<td>18.6 ± 1.1</td>
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<tr>
<td>D_{95} (Gy)</td>
<td>26.0 ± 2.9</td>
<td>22.8 ± 1.0</td>
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<td>22.2 ± 1.0</td>
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<td>Liver</td>
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<td>D_{\text{med}} (Gy)</td>
<td>24.4 ± 6.3</td>
<td>22.8 ± 10.1</td>
<td>0.44</td>
<td>29.2 ± 2.0</td>
<td>0.09</td>
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</table>

\textit{Abbreviations:} IMAT = intensity-modulated arc therapy; CONV2 = conventional plan with an anteroposterior and a posteroanterior field; CONV4 = conventional plan with four-field technique; PTV = planning target volume; PTV_optim = PTV without build-up region of 0.8 cm and with the exclusion of the expanded kidneys with an extra margin of 5 mm; \text{V}_{95}, \text{V}_{90}, \text{and} \text{V}_{107}: \text{the partial volume (percent) receiving more than 95\%, 90\%, and 107\% of the prescribed dose, respectively; } D_{90} \text{ and } D_{1} = \text{Dose given to 99\% and 1\% of the volume, respectively; } U_{95/5} = \text{inhomogeneity factor, defined as } \frac{(D_{99} - D_{1})}{D_{\text{med}}}, \text{with } D_{95} \text{ the 95th percentile dose; } D_{5} \text{ the 5th percentile dose, and } D_{\text{med}} \text{ the median dose.}
RESULTS

The median volume of the PTV in the 5 patients was 8306 cc (range 5717–9054 cc), and the median of the craniocaudal length which had to be covered was 36 cm. Details on the treatment plans and delivery times are shown in Table 1. Mean delivery time for Patients 2–5 was 13.8 min (range 9.5–24.5 min). Less than 30% of the given fractions had a delivery time exceeding 15 min. Of these, 50% were seen in Patient 4, who had two isocenters, necessitating entrance of the treatment room to perform a cranial shift of the patient. For 1 patient (chronologically the last), the setup time was measured over all the fractions, and showed a mean of 8 ± 2.9 min. Though actively asked, no patient complained about the rotating gantry. As an example, the obtained intensity profiles for Patient 5 are shown in Fig. 4.

DVH analysis and dose distributions

The DVH data for the 5 patients are summarized in Table 2 and graphically displayed in Fig. 5. For both the CONV4 and IMAT plans, there is a large variation in minimal dose (represented by D1) in the PTV (range 0.2–26.1 Gy), resulting from the PTV extending outside the skin in 1 patient. When considering the PTV without a build-up region of 8 mm (PTV_whbu), the very low doses that are the result of the ICRU PTV definition rather than of the planning technique are eliminated (range of D1 19.5–26.9 Gy). The homogeneity in the PTV_whbu is better for the IMAT plan than for the CONV4 plan (U 95/5 is 20% and 32%, respectively; p < 0.01). Because of the strong dose constraint to the expanded kidneys and the possibility to generate concave dose distributions, we expected an underdosage in the PTV in the region around the kidneys. For the PTV_optim, the mean (and the standard deviation) of the V95 was 78.4% (± 2.2%) for the CONV4 plan, and 88.9% (± 5.1%) for the IMAT plan (p = 0.01). For the V90, these values were 87.7% (± 3.0%) and 95.8% (± 3.5%) for the CONV4 and the IMAT plan, respectively (p = 0.02). The comparison between the IMAT plan and the CONV2 plan

Fig. 5. DVHs compiled from the data of the 5 patients. Solid lines and bold dots represent the IMAT plans (mean ± standard error of the mean). Dashed lines and circles represent the 2D plans. (a-c) DVHs of the IMAT and CONV2 plans. (d-f) DVHs of the IMAT and CONV4 plans. (a) + (d) DVHs of PTV and expanded left kidney. (b) + (e) DVHs for PTV_whbu and expanded right kidney. (c) + (f) DVHs of PTV_optim and liver.
(see Table 1) shows a significant increase in homogeneity (expressed by $U_{95/5}$) for the PTV and for PTV_optim by the IMAT plans.

The median dose to the kidneys was lower for the IMAT plan in all patients when compared with both CONV plans. The maximal doses to the kidneys were significantly higher for the IMAT plan than for the CONV plans, as can be seen in Fig. 5. For the liver, no significant differences were found between the IMAT and the CONV plans. The higher homogeneity by the use of lateral beams in the CONV4 plans yielded a higher dose to the liver.

Dose distributions for the first patient are shown in Fig. 6. The sparing of the kidneys by the IMAT plan does not produce underdosages in the cone of the PTV lying anteriorly to the kidney, in contrast to the CONV2 plan (see Figs. 6b and 6e). This underdosage is largely, but not completely, resolved in the CONV4 plan, at the cost of higher liver dose (see Figs. 6c and 6f). The dose distributions also illustrate that the maximal doses to the kidneys were higher in the IMAT plans than in the CONV plans, because there is a steep circular gradient around the kidneys.
Intensity modulation gives the possibility to generate concave dose distributions. This is a major advantage in the treatment of cases in which the PTV is wrapped around a concave dose distribution. This is a major advantage in the treatment of cases where the radius of curvature of the concavity is larger than the setup error (e.g., in the head-and-neck region). For planning cases where the radius of curvature of the concavity is larger than the setup error, Stein et al. (23) demonstrated this for prostate cancer where the dose distribution concavity is generated around the rectum. For PTV, 1.2% of the volume had a $\gamma$-index $>1$. An example of a computed and a measured dose distribution is shown in Figs. 8a and 8b, respectively, together with the iso-$\gamma$ line at value 1 (Fig. 8c).

**DISCUSSION**

Intensity modulation gives the possibility to generate concave dose distributions. This is a major advantage in the treatment of cases in which the PTV is wrapped around a dose-limiting OAR (e.g., in the head-and-neck region). For planning cases where the radius of curvature of the concavity of the intended isodose lines is rather small, a beam setup with a limited number of incidences is sufficient. Stein et al. (23) demonstrated this for prostate cancer where the dose distribution concavity is generated around the rectum. However, when the internal radius is increasing with equal distance to OARs inside the concavity, an increasing number of beam incidences is needed to avoid underdosage in parts of the PTV while maintaining the same OAR sparing, as demonstrated in Fig. 9. The fastest way to deliver a very large number of incidences is arc therapy. Therefore, IMAT was selected in our department as a delivery method only for those situations in which intensity modulation is needed together with sparing of OARs of medium and large sizes.

Next to WAPRT, the same planning problem can be encountered in, for example, rectal cancer (and more broadly in pelvic irradiation), malignant pleural mesothelioma, and breast cancer.

We compared the planning results of the IMAT plan with a two-field and a four-field conventional plan. By applying IMAT, we could improve homogeneity ($U_{5/5}$) by 49% in the PTV without build-up region of 0.8 cm and with the exclusion of the expanded kidneys with an extra margin of 5 mm.

**Table 3.** Total volumes of contoured structures, volumes of the parts of these structures inside the gel phantom, and relative volumes of these parts (percentage volumes of the truncated structures that have a $\gamma$-index above unity are shown in the last column)

<table>
<thead>
<tr>
<th>Structure</th>
<th>Volume (cc)</th>
<th>Volume in gel phantom (cc)</th>
<th>Partial volume in gel phantom (%)</th>
<th>Volume ($\gamma &gt;1$) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>6943.2</td>
<td>2060.9</td>
<td>29.7</td>
<td>1.2</td>
</tr>
<tr>
<td>PTV_optim</td>
<td>6574.8</td>
<td>1907.9</td>
<td>29.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Left kidney (expanded)</td>
<td>370.8</td>
<td>337.5</td>
<td>91.0</td>
<td>8.3</td>
</tr>
<tr>
<td>Right kidney (expanded)</td>
<td>283.6</td>
<td>254.4</td>
<td>89.7</td>
<td>19.6</td>
</tr>
<tr>
<td>Liver</td>
<td>1471.6</td>
<td>1459.0</td>
<td>99.1</td>
<td>1.9</td>
</tr>
<tr>
<td>Scanned volume</td>
<td>18653.8</td>
<td>8330.7</td>
<td>44.7</td>
<td>8.1</td>
</tr>
</tbody>
</table>

Abbreviations: PTV = planning target volume; PTV_optim = PTV without build-up region of 0.8 cm and with the exclusion of the expanded kidneys with an extra margin of 5 mm.
Fig. 7. (a) Dose–volume histograms of the computed (solid lines) and gel-measured (dashed lines) dose for the contoured volume inside the gel. C1-6: clinical constraints, with C1: more than 95% of the volume of the PTV_optim has to receive more than 90% of the prescribed dose; C2: less than 5% of the PTV may receive more than 107% of the prescribed dose; C3: less than 5% of the expanded kidneys may receive more than 25 Gy; C4: less than 20% of the expanded kidneys may receive more than 30 Gy; C5: median dose to the expanded kidneys should be lower than 18 Gy and C6: median dose to the liver should be lower than 30 Gy. (b) Volume histogram using the computed $\gamma$-index. The thick line represents the total measured volume.
by MR further can contribute to differences seen between measurements and calculations and will be investigated.

Hong et al. (11) described the planning results for WA-PRT using static gantry IMRT with five incidences. The delineation of the target volumes and OARs were quite similar to those described in this report. Hong’s treatment planning goal differs by the use of the unexpanded kidneys as OARs. The mean \( V_{95} \) of the PTV was 83.5\% for the static IMRT, whereas it was 82.2\% in our study. However, in the report by Hong et al., the overlap with the kidneys was excluded from the PTV. When we look at the PTV_optim, which also excludes the overlap region, the mean of the \( V_{95} \) was 88.9\%. These data reflect that the dose homogeneity in the PTV is similar for both planning techniques. The mean dose to the kidneys is also in the same range in both reports. In the report of Hong et al., a mean of 1442 MUs was needed for a fraction of 150 cGy, where IMAT resulted in 444 MUs on average for the same dose. Because of the design of the Varian MLC, for which Hong’s implementation was intended, a split of the intensity-modulated fields was necessary, which gives rise to a higher number of MUs. Hong did not report on delivery time.

IMAT with dynamic multileaf collimation was first described by Yu (8). Yu initially reported on an IMAT planning methodology using inverse planning (Peacock, NOMOS Corporation, Sewickley, PA). Optimized beam fluences were “decomposed” to multiple superimposing fields. In the inverse planning strategy described by Yu, the intent is to generate control points that are compliant with the MLS constraint with regard to the previous control point of the arc. If such a decomposition can’t be found, Yu described a softening of the MLS constraint with selection of a lower nominal dose rate. The Elekta SLi-18 picks a nominal dose rate from a set of discrete values (32, 65, 130, 260, or 520 MU/min) so that the gantry speed is as close as possible to 156°/min (range 104–208°/min). We were unable to apply Yu’s method because we could not influence the selection of this nominal dose rate without elimination of safety interlocks. In our implementation, the MLS constraint is handled using a combination of anatomy-based segmentation and the LVC. For volumes of interest at maximum 12.5 cm of a cranio-caudal axis through the isocenter, it can be proven that the lateral position of their projected outlines in BEV between two adjacent incidences, interspaced by 8°, can, in the worst case, only differ 2.0 cm when beam divergence is not taken into account. Because the Elekta MLC has a possible overtravel distance up to 12.5 cm for all leaves, and leaf speeds are sufficient to move 2.0 cm each 8° of arc rotation, the conformal avoidance of OARs within the previously mentioned regional constraint is always possible. For volumes of interest as the PTV that do not fit within the 12.5-cm cylinder, anatomic boundaries in BEV can have higher lateral shifts. For volumes within 20.0 cm of the longitudinal axis, this can amount up to 3.5 cm, which is only obtained in the worst-case scenario. By beam divergence, larger lateral shifts can

![Fig. 8. Dose distributions in the middle transverse plane of the Barex cast (Fig. 3) for the IMAT plan, (a) as calculated with the collapsed cone convolution/superposition algorithm from Pinnacle and (b) as measured by monomer/polymer gel dosimetry. For (a) and (b) isodoses are shown at 3 Gy intervals. (c) Iso-γ line for γ = 1. PTV: planning target volume (dotted line). The liver is indicated with a dashed-dotted line, the kidneys with a dashed line.](image-url)
occur. Where the MLS constraint would be violated in the process of machine state generation, it was resolved by the LVC. Recently, the first clinically delivered planning results of IMAT were published (25, 26). In both reports, a planning strategy was used in which the outlines of the machine states were based on patient anatomy. The initial reports, using anatomy-based segmentation could indicate that the inverse planning method described by Yu (8) is hard to implement in clinical practice. To deal with the problem of MLS, they had to insert a wedge in (some) arcs to increase the number of MU per degree of arc rotation (26). In our opinion, wedges are superfluous in IMAT planning, because this procedure decreases MU efficiency and because the leaf speed problem can be solved by optimization methods.

The clinical implementation of IMAT for this site was a challenge for other than plan and technical reasons too. The setup procedure was strongly influenced by the combination of the large target volume and the limitations of the Elekta table. The C-arms can only be set in a nonhorizontal position (120°) if the table is sufficiently extended longitudinally toward the gantry drum. The distance in caudal direction between the isocenter and metal components of the support system in this extended position is maximally 26.4 cm. Because the PTV has a median height of 36 cm, repositioning range in a cranio-caudal direction using the table shift possibility was restricted. This is a problem that occurs when a static incidence technique was used unless care was taken to generate only segments that can be delivered with the bars in either the most lateral or medial position. For a PTV of the previously mentioned sizes, this will, in practice, lead to a restriction of possible gantry angles or delivery of the treatment in two parts (one for each bar position). During the planning process, the maximal arc range was used, taking a 2-cm margin between table bars and field aperture in lateral direction into account. Repositioning using the motorized table shift system in this direction was therefore restricted to an uncommonly small range. As a consequence, the table had to be set to predefined lateral and longitudinal positions, after which the first positioning was done by shifts of the patient relative to the table. The support system capabilities were used to correct for the last millimeters of the patient setup. A shorter setup time could be achieved by use of an appropriately designed carbon fiber table top.

To implement IMAT (8 patients currently) in the same routine clinical practice as IMRT (in total, 362 patients, 120 in 2002, which is ± 10% of our patient load), further automation is necessary on several points. The transition of virtual to deliverable arcs is a time-consuming manual operation. Although a class solution can aid the planner toward a final arc setup, constraints on the modulation of the angular delivery rate during optimization would reduce the problem. Full automation of this procedure would be optimal. Start-and-stop angle optimization can fine tune converted arcs. The conversion of arcs with a nonconstant angular delivery rate could be avoided by a variable gantry speed. This could enhance planning quality, reduce the number of arcs and the delivery time, and decrease planning complexity by eliminating the conversion and elimination of local minima induced by the discretization. Although the Elekta linac has excellent mechanical possibilities to achieve this through its rotation mechanism, Elekta was not yet able to implement a variable angular delivery rate for IMAT.

CONCLUSION

We clinically applied five IMAT treatment plans for WAPRT. IMAT was validated dosimetrically and was
shown to be deliverable in an acceptable time slot and to produce dose distributions that are significantly more homogeneous at the PTV than those obtained with a CONV plan. Our anatomy-based segmentation strategy offered a feasible solution in view of the leaf speed constraint. Although the planning is still time-consuming, we think this can be solved by adaptations to the patient couch, the control software of the linear accelerator, and the planning software—each of which has the potential to improve the quality of the IMAT plans.

REFERENCES


