JBUON 2015; 20(1): 196-205
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

The first implementation of IMRT technique for head & neck and prostate cancer patients in public sector in Greece: feasibility, treatment planning and dose delivery verification using the delta^{4PT} Pre-Treatment volumetric quality assurance system

Vassilis Kouloulias[1,2], Christos Antypas[1], Zoi Liakouli[1], Christina Armpilia[1], Anna Zygogianni[1], Ioannis Floros[1], Maria Tolia[1], John Kokakis[1], John Kouvaris[1]

[1]*"Aretaieion" University Hospital, 1st Department of Radiology, Radiotherapy Unit, Medical School, National Kapodistrian University, Athens;* [2]*"Attikon" University Hospital, 2nd Department of Radiology, Radiotherapy Unit, Medical School, National Kapodistrian University, Athens, Greece*

Summary

Purpose: *Intensity Modulated Radiation Therapy (IMRT) is nowadays the treatment of choice, in terms of technique, for either head & neck or prostate cancer. With this paper, we are sharing our experience for the first inplementation of IMRT planning in the public sector in Greece, and especially in the Aretaieion University Hospital of Athens.*

Methods: *From May 2013 until January 2014 four prostate and four head & neck cancer patients were evaluated in the present study. We used the ONCENTRA IMRT treatment planning with a step and shoot technique in a SIEMENS ONCORE Linac. The dose verification method used was based on the delta4^{PT} Pre-Treatment volumetric quality assurance system, by Scadidos.*

Results: *In all cases, the Relative Standard Deviation between the prescribed and the calculated average dose received by the target volume was less than 5%, while the γ-index was more than 90%. The acute toxicity was low and equivalent to published data with IMRT technique.*

Conclusion: *In conclusion, the first implementation of IMRT technique in the Medical School of Athens was feasible and safe as well as in terms of dose verification. The IMRT technique is already in clinical use and further results with long term radiation induced toxicity will be reported.*

Key words: *dose verification, dosimetry, feasibility, IMRT, radiotherapy, toxicity*

Introduction

Head & neck and prostate cancer require high doses of radiotherapy (RT) to achieve local control, in the range of 70 Gy for head & neck and 78 Gy for prostate cancer. The main concern when raising the dose of RT is the toxicity from the surrounding normal organs and tissues. Zelefsky et al. reported a 10-year incidence of grade 2 or more gastrointestinal (GI) toxicity of 13% in prostate cancer patients that were treated with conventional 3-dimensional conformal radiotherapy (3D-CRT) [1]. In the Dutch multicentre randomized trial for prostate cancer, a statistically significant difference in 7-year freedom from failure (FFF) was observed in the high dose group (56 vs 45%, p=0.03), but with an increase in the cumulative incidence of late grade 2 or greater GI toxicity (35 vs 25%, p=0.04) [2,3]. Intensity Modulated Radiation Therapy (IMRT) is a technique that offers the ability to create a dose distribution with high precision around the target volume while protecting the surrounding normal tissues [4,5]. The main clinical goals when using IMRT in prostate

Correspondence to: Vassilis Kouloulias, MS, MD, PhD. "Attikon" University Hospital, 2nd Department of Radiology, Radiotherapy Unit, Rimini 1, Chaidari, 12462, Athens, Greece. Fax: +30 210 5326418, E-mail: vkouloul@ece.ntua.gr
Received: 16/08/2014; Accepted: 01/09/2014

and head & neck cancer are reduction of treatment related toxicity and improvement in disease free survival (DFS) [6-8].

Especially in the case of head & neck cancer, with the combination of RT and chemotherapy, there may be interruptions in the therapy, dose reduction and diminished quality of life of patients, due to toxicity of the therapies. Xerostomia is one of the main side-effects that influences the patient's well-being [9,10]. For these reasons, the implementation of IMRT in head & neck cancer, with the highly conformal dose distribution that is achieved, is very promising and is tested in phase III trials [11-17]. Nutting et al. reported a statistically significant difference in xerostomia for patients with oropharyngeal cancer that were treated with IMRT compared with 3D-CRT (41 vs 64% of grade 2 xerostomia) [11]. Similar results were found in nasopharyngeal cancer, with Kam et al. reporting 39% grade 2 xerostomia at 1 year with IMRT vs 82% with 2D RT [12]

IMRT can be delivered either with a dynamic multileaf collimator technique (MLC) or with a step-and-shoot technique, the first delivering the dose while the leaves are moving, and the second with static leaves in each segment of the multiple fields. Adams et al. comparing the two methods found that they both are accurate and reproducible in the treatment delivery [18] and similar results were reported by Alaei et al. [19]. With regard to differences in monitor units (MU) delivered and overall treatment time, Chui et al. reported that step-and-shoot approach requires 20% less MU [20], while Adams et al. reported that treatment delivery time is slightly shorter with the static technique (average time 10 vs 14 min) [18]. Increased treatment time and number of monitor units raise the question of the percentage of healthy surrounding tissues that receive low doses and the clinical impact that could have in radiation-induced malignancies. Jothybasu et al. reported an increase in the integral dose to the healthy tissues with dynamic MLC, but that was not statistically significant [21].

Quality assurance (QA) is the main aspect of verifying the dose delivering to the human body during irradiation [22]. The need of QA is rising dramatically when the IMRT technique is used. Several methods of QA have been used for dose verification, such as film dosimetry, thermoluminiscent detectors (TLDs), polymeric gels and volumetric systems [23-28].

Recently, the Delta4PT pre-treatment system as a volumetric QA system has been installed in our department for routine QA in IMRT treatment planning verification [29].

The aim of the present study was to report on the first implementation of IMRT treatment planning for prostate and head & neck patients in the public sector in Greece at the Aretaieion University Hospital of Athens. Moreover, the clinical efficacy along with the QA method for dose verification is also reported.

Methods

Patient characteristics – dose prescription

From May 2013 until January 2014 4 prostate and 4 head & neck patients (one laryngeal, one tonsilar and two nasopharyngeal carcinomas) were evaluated in the current study. Detailed medical history of the 8 patients is described below:

The first patient (case A) was a 56-year-old male, who in a regular checkup in 2009 had a PSA value of 4 ng/ml. Magnetic resonance imaging of the prostate was negative for either extracapsular or nodal invasion. In April 2011, PSA was 8.4 ng/ml. At that time, he received treatment with antibiotics for prostatitis and PSA fell to a value of 6.4 ng/ml. In September 2012, PSA was 6 ng/ml. A biopsy of the prostate was then performed by means of 10 samples from the right lobe and 15 from the left lobe. Histology showed that all samples from the left lobe and 2 from the right lobe were infiltrated from an adenocarcinoma of the prostate with a combined Gleason score 6 (3+3). There were also areas of high grade PIN. The patient received 78 Gy to the prostate and 54 Gy to the seminal vesicles.

The second patient (case B) was a 75-year-old male, with a gradual rise in PSA from 4.5 ng/ml in 2011 to 8.6 ng/ml in January 2013. Digital rectal examination (DRE) revealed an area of mild induration and ultrasound of the prostate showed an increase in the size of the organ and inhomogeneity of the peripheral zone. A biopsy was taken under ultrasound guidance and the histologic examination showed adenocarcinoma of the prostate, Gleason score 6 (3+3) in one of the 8 samples from the right lobe. The rest of the imaging studies (bone scan, CT and MRI of the pelvis) was negative for either metastasis or involved lymph nodes. The patient received 76 Gy to the prostate and 54 Gy to the seminal vesicles.

The third patient (case C) was a 45-year-old female, who in February 2013 realized a deterioration concerning smell and taste, while in a short period of time there was a decrease in hearing ability. She consulted an otorhinolaryngologist and the clinical examination revealed a palpable mass in the left cervical region. MRI study of the head & neck area showed pathologic signal in the nasopharynx and involved (<6 cm) cervical and supraclavicular lymph nodes. A biopsy of the nasopharynx was then performed, which showed infil-

tration from an undifferentiated squamous cell carcinoma. Expression of the Epstein-Barr virus genome was noticed. The rest of imaging study with CT of the thorax and abdomen was negative for any distant metastasis. The patient received 70 Gy to the nasopharynx, 66 Gy to the involved cervical lymph nodes, 54 Gy to the uninvolved cervical lymph nodes and 50 Gy to the supraclavicular fossa.

The fourth patient (case D) was a 69-year-old male, who presented with hoarse voice. The clinical examination from an otorhinolaryngologist revealed a supraglottic lesion with extension to the glottic larynx and fixation of the vocal cord. CT and MRI of the neck confirmed the above findings with no involved regional lymph nodes. A biopsy taken from the supraglottis showed a squamous cell carcinoma of moderate differentiation (grade II). The rest of the imaging study with CT of the thorax and abdomen was negative for distant metastasis. The patient received 70 Gy to the larynx, 54 Gy to the cervical lymph nodes and 50 Gy to the supraclavicular fossa.

The fifth patient (case E) was a 51-year-old male who presented with difficulty in swallowing, palpable cervical lymph nodes and weight loss of 10 kg in the last 3 months. CT and MRI scans of the neck showed abnormality in the right tonsillar fossa. Multiple infiltrated nodes were shown in both sides of the neck. The patient underwent endoscopy which confirmed the findings by means of a lesion in the right tonsil. Biopsies taken from the right tonsil and from one of the involved lymph nodes on the right cervical region showed a poorly differentiated squamous cell carcinoma. The rest of the imaging was negative for distant metastasis, by means of a CT scan of the thorax and abdomen. The patient received 66 Gy to the primary tumor and involved lymph nodes and 54 Gy to the high-risk areas.

The sixth patient (case F) was a 61-year-old male who in a regular checkup in February 2013 had a PSA value of 26.5 ng/ml. A biopsy of the prostate taken under ultrasound guidance revealed adenocarcinoma, Gleason score 6 (2+4), with infiltration of both lobes. The rest of the imaging in terms of CT scan of the pelvis and bone scan was negative for metastasis or involved lymph nodes. The patient underwent radical prostatectomy and the histology showed an adenocarcinoma, Gleason score 9 (4+5), infiltrating both of the lobes and the seminal vesicles. There was also extension in the periprostatic fatty tissue. The surgical margin of the apex of the gland was infiltrated. The patient received 44 Gy to the pelvic lymph nodes and 70 Gy to the surgical bed of the prostate and seminal vesicles.

The seventh patient (case G) was a 77-year-old male who in a regular checkup had a PSA value of 42 ng/ml. A biopsy under ultrasound guidance was taken by means of 6 samples from the right lobe and 12 from the left lobe. The histological examination revealed an adenocarcinoma of the prostate, Gleason score 8 (4+4), with infiltration of 4 samples from the right lobe and 1 from the left lobe. The patient underwent a CT scan of the abdomen which showed an increase in the size of the prostate and a bone scan which was negative for metastasis. The patient received 45 Gy to the pelvic lymph nodes, 55 Gy to the seminal vesicles and 74 Gy to the prostate.

The eighth patient (case H) was a 42-year-old male who presented with palpable cervical lymph nodes. An FNA of one of the left cervical lymph nodes was performed and the cytological examination showed infiltration from a high grade squamous cell carcinoma, probably from the nasopharynx. The patient underwent an MRI of the nasopharynx and neck which revealed pathologic signal in the left side of the nasopharynx and multiple infiltrated lymph nodes in both sides of the neck. In clinical examination paresis of the sixth cranial nerve was discovered. A biopsy from the nasopharynx showed a non keratinizing differentiated carcinoma of the nasopharynx. The rest of the imaging by means of a CT scan of the thorax and the abdomen was negative for distant metastasis. The patient received 70 Gy to the nasopharynx, 66 Gy to the involved lymph nodes and 54 Gy to the high risk areas.

Radiotherapy technique - Prostate

Each patient underwent a CT-simulation, in supine position, using "knee sponge" to consistently align thighs [30].

Patients were instructed to have a full bladder and empty rectum (following a dietary suggestion) during simulation and the whole course of treatment. For treatment planning, a CT scan covering a region from the first lumbar vertebra to the lower part of the perineum was obtained for each patient.

All contouring of target volumes and normal structures (organs at risk-OARs) was performed in the Oncentra Treatment Planning System. MRI and CT images were obtained at 3-mm intervals. The CT and MRI were registered by the Oncentra system while corrections were made in the CT-based contouring of the prostate by taking into account the MRI images. The following structures were delineated: clinical target volume (CTV), planning target volume (PTV) according to the ICRU criteria, based on the anatomical structures of CT images and clinical parameters [31-35].

The PTV was obtained by expanding CTV with a margin of 1 cm in each direction, and of 0.7 cm posteriorly [36-38].

The dose constrains used in our study were according to the QUANTEC study [18,19] as follows:

Rectum: D50 <50 Gy, V60 <35%, V65 <25%, V70 <20%, V75 <15%

Bladder: V65 <50%, V70 <35%, V75 <25%

Penile bulb: mean dose to 95% of the gland <50

Small bowel: V45 <195cc

The prescription dose was defined for the 95% iso-

doses of the PTV. The IMRT plans were created using the Oncentra External Beam v4.3 treatment planning system, by Nucletron. The collapsed cone convolution algorithm was used during optimization and the final dose calculation. The performed plans were evaluated using the Delta4PT pre-treatment system by Scandidos [29].

Radiotherapy technique – Head & Neck

Each patient underwent a CT-simulation, in supine position, using an immobilization mask. All contouring of target volumes and normal structures (organs at risk/OARs) were performed in the Oncentra Treatment Planning System. MRI and CT images were obtained at 3-mm intervals.

The gross tumor volume (GTV) definition for irradiation included the tumor itself and the positively diagnosed lymph nodes, by using registered images of MRI performed with the Oncentra System. A margin of 1.5 cm was applied to GTV in order to include the CTV. In all patients, elective areas with a reasonable risk for microscopic disease, such as the ipsilateral or contralateral neck levels, were defined as different CTVs [39-41].

In patients who underwent surgery, the CTV included the surgical resection bed with 1.5 cm safety margins. A margin of 3–5 mm was applied on all CTVs in order to define the PTV and on account of setup and treatment delivery uncertainty [42-44].

The dose constrains used in this study were according to the QUANTEC study [47,48] as follows:

Spinal cord Dmax =50

Brainstem Dmax <54, D1-10cc <59

Optic chiasm/nerve Dmax <55

Parotid mean dose <25 (bilateral whole parotid glands)

Cochlea mean dose <45

Pharyngeal constrictors mean dose <50

The Delta 4PT QA device

The Delta 4PT device by Scandidos is a volumetric cylindrical 3D phantom with 22 cm diameter, constructed of PMMA and designed in two orthogonal planes [29]. The one plane is referred to as the main board by the device's specifications and the other as the wings (Figure 1). The two planes are separated from the vertical plane by +50° for the main board and by -40° for the wings. The two planes are not located in equally crossed directions, as the beam alignment with the one or the other plane must be avoided [45]. The phantom's dosimetric system consists of a total of 1069 p-type silicon (Si) detectors with a spatial resolution of 5 mm in the centre and 10 mm in the outer phantom area, while the dose resolution is of 0.01mGy and the dose response threshold is of 1 mGy. The detectors' active volume is 1 mm in diameter and 0.05 mm thick. The

Figure 1. The Delta 4PT phantom used for dose verification

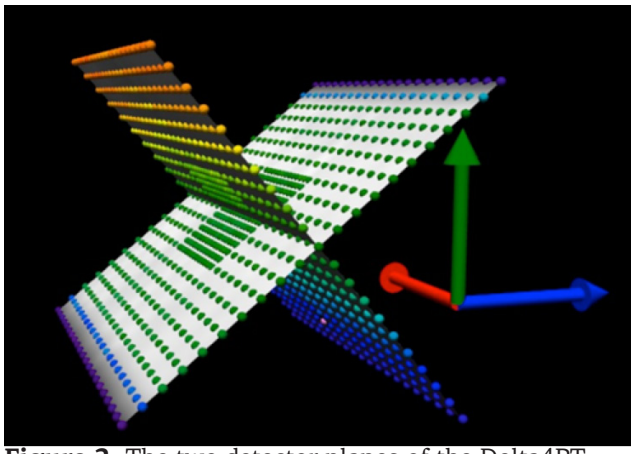

Figure 2. The two detector planes of the Delta4PT phantom by Scandidos. Different colors indicate the deviation between planned and delivered dose.

two detector planes are connected with multichannel electrometers and the measured data are synchronized with the accelerator pulses and stored on a pulse-by-pulse basis, allowing segment-by-segment analysis and 4D treatment QA [46]. The system utilizes an algorithm that calculates, with high accuracy, the precise numerical values of the spatial dose distribution, providing statistical comparisons between the outlined and the performed treatment plan (Figure 2).

Treatment planning evaluation

The current work presents an assessment of the IMRT treatments performed in our department. The evaluation of the overall procedure is divided in two parts.

The first part refers to the clinical part and the ability of the treatment planning algorithm to meet all the constraints defined for the tumor target and the OARs during the optimization using the mlc specifications and commissioning beam data for IMRT treatments. The second part is based on the dosimetric comparison between the calculated and the deliverable IMRT plan.

Table 1. Treatment planning verification for prostate cases

Case	*Volume*	*Pre. dose*	*D_{ave} (Gy)*	*RSD %*	*V50 %*	*V65 %*	*V75 %*	*γ-index %*
1	PTV	70.00	72.1	3				97.70
	Rectum				35.8	13.6	-	
	Bladder				-	14.3	-	
2	PTV	77.00	79.0	3				97.30
	Rectum				35.4	13.9	-	
	Bladder				-	33.5	17.5	
3	PTV	72.00	75.9	5				95.40
	Rectum				43.4	13.9	-	
	Bladder				-	41.1	13.8	
4	PTV	70.00	72.1	3				97.60
	Rectum				25.1	4.7	-	
	Bladder				-	14.8	-	

PTV: planning treatment volume, Pre.dose: prescribed dose, Dave: average dose, RSD: relative standard deviation, V_x%: percentage of the volume with x dose

Table 2. Treatment planning verification for head & neck cases

Case	*Volume*		*Pre. dose*	*Dave (Gy)*	*RSD (%)*	*Dmean(Gy)*	*γ-index (%)*
1	PTV		70.00	70.18	0.26		90.8
	Parotid gland	left				28.46	
		right				27.39	
2	PTV		70.00	69.29	-1.01		91.0
	Parotid gland	left				31.97	
		right				29.47	
3	PTV		70.00	71.59	2.27		92.5
	Parotid gland	left				54.76	
		right				56.20	
4	PTV		66.00	68.74	4.15		95.4
	Parotid gland	left				57.76	
		right				59.35	

For abbreviations see footnote of Table 1

The above described evaluation method includes several dosimetric variables calculated in the treatment planning system for the tumor target and the OARs, as well as variables measured using the Delta 4 volumetric phantom, the latter presenting the statistical accordance of the calculated with the deliverable IMRT plan. In detail, for each case the variables applied during the evaluation are as follows:

- $D_{average}$ defines the calculated average dose received by the target volume
- RSD %, is the Relative Standard Deviation between the prescribed and the calculated average dose received by the target volume
- V50, V65 and V75 define the volume limit for 50, 65 or 75 Gy of delivered dose for the OAR, recommended by QUANTEC [47,48]. For the prostate cases the rectum and bladder were considered as the OARs with the following dose to volume limits : rectum, V50 < 50% and V65 < 25 %, bladder, V65 ≤ 50% and V75 ≤ 25%. For the head and neck cases the mean dose limit for every parotid gland was determined <20 Gy.
- γ-index is the standard statistical method for planar dose verification in IMRT QA and is determined by the ratio of the dose difference (DD) and the dose to agreement (DTA) between the outlined and the measured plan for each point of interest

Table 3. Acute radiation induced toxicity for prostate and head & neck cases. The evaluation for toxicity was performed with the EORTC/RTOG scaling (grade I-IV), while for prostate with the SRS scale (score range: 0-8) was also used

Case	*Acute EORTC/RTOG toxicity*					*SRS score*
	Skin	Mucositis	Xerostomia	Urinary	Rectal	
A (prostate)	none	-	-	I	I	1
B (prostate)	I	-	-	II	I	2
C (nasopharynx)	I	II	I	-	-	-
D (larynx)	II	II	I	-	-	-
E (tonsil)	II	I	I	-	-	-
F (prostate)	I	-	-	I	I	2
G (prostate)	I	-	-	I	II	1
H (nasopharynx)	I	II	I	-	-	-

[49,50]. The confidence limit for γ-index criterion expresses the percentage of γ-values ≤ 1 and is automatically calculated for 3% dose difference and 3 mm distance to agreement (3%/3 mm) by the Delta 4 software.

The pre-treatment QA process using the Delta4PT phantom was followed for the γ-index calculation. Prior to the "field by field" verification process per application [51], a specific procedure for the daily dosimetric corrections of the device and the positioning optimization was followed. For this purpose the air temperature was added in the Delta4 software and two irradiations with 10×10 cm^2 field in orthogonal configuration at 0° and 90° degrees were performed. The software's positioning corrections were applied and the plans were delivered. For all cases, a plan is considered to be successful if more than 90% of the tested diodes pass the gamma test.

Clinical evaluation

All patients were followed up for 6 months post irradiation. For prostate patients the follow up included PSA values and evaluation of acute rectal toxicity using a subjective-objective scale based also on rectosigmoidoscopy (SRS) [52]. For head & neck patients, the follow up included clinical examination and MRI. In all cases the acute toxicity was also assessed with the EORTC/RTOG acute toxicity scale [53].

Results

Dose verification

Results of patient plans verification for the two evaluated anatomical sites are summarized in Tables 1 and 2. For the prostate cases the RSD between the prescribed and the calculated dose was ≤5% and the calculated variables V50, V65 for rectum and V65, V75 for bladder were lower compared to the recommended limit. Regarding the IMRT pre treatment's plan verification with the Delta 4^{PT} phantom the average γ-index was >97%. For the head and neck cases the RSD was <5%, while the delivered mean dose to the parotid glands exceeded the recommended limit by QUANTEC. The average γ-index for all cases was >90%.

Clinical outcome

All patients completed their treatment without any interruption. The mean treatment time (patient setup, EPID verification and beam-on) was 25 min (range 21-35). The acute radiation induced toxicity is shown in Table 3. No grade II or higher acute toxicity was noted either for prostate or for head & neck cases. One prostate patient complained only for discomfort in the anorectal function combined with spotted blood due to hemorrhoid's inflammation. The PSA level for all prostate patients was decreased at 3 months post irradiation by a mean value of 0.55 (range 0.22-0.8). In all head and neck cases the saliva function was decreased, but without any grade II or higher xerostomia. Two typical IMRT plannings for prostate and head & neck cases are shown in Figures 3 and 4, respectively.

Discussion

IMRT is an advanced RT technique that delivers higher doses to the tumor target, satisfying at the same time strict constraints for the OARs. This is of great importance in many cancer types which require high doses in order to achieve better local control. Zelefsky et al. in a total of 561 patients with prostate cancer treated up to 81 Gy reported 8-year actuarial PSA relapse-free survival rates for patients with favorable, intermediate and high risk features of 85, 76 and 72%, respectively [6]. Gastrointestinal (GI) and genitourinary

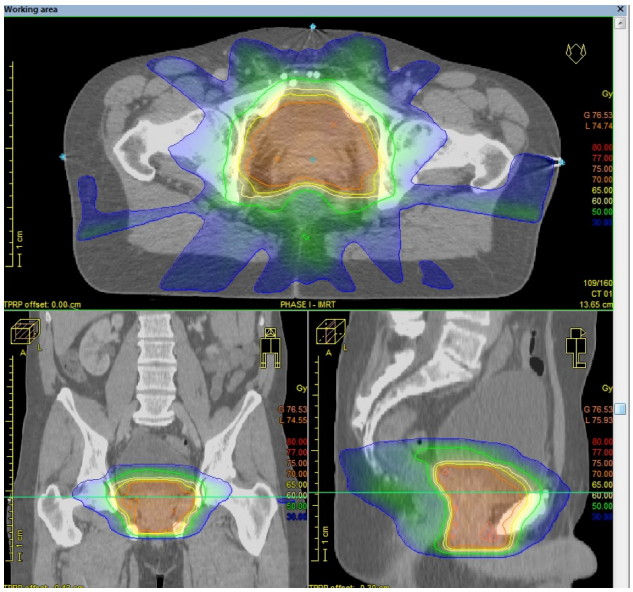

Figure 3. A typical dose-mesh distribution related to the isocenter for case A (prostate cancer).

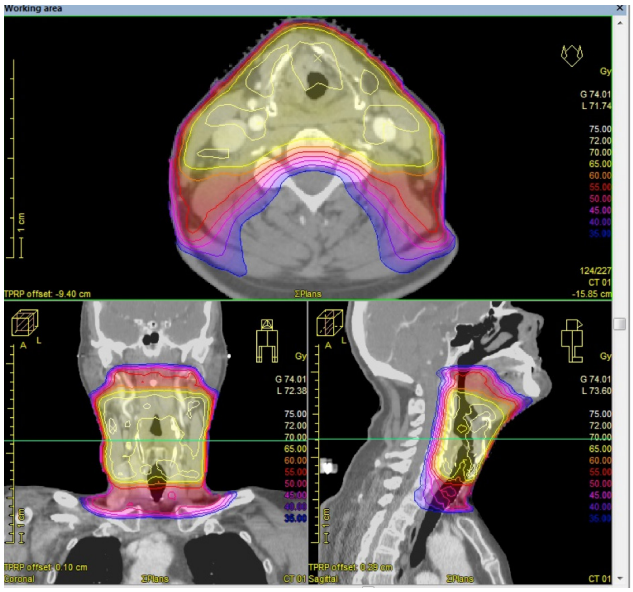

Figure 4. A typical dose-mesh distribution related to the isocenter for case E (head & neck cancer).

(GU) toxicity, acute and late, are of main interest when treating patients with prostate cancer with high doses [3]. Acute GI and GU toxicity in our study, with only one patient developing acute grade II urinary and one acute grade II rectal toxicity, are in accordance with the figures published in the literature. Peeters et al. reported in the first results of the Dutch multicenter trial for prostate cancer acute grade II GI and GU toxicity in 44% and 41% of their patients, respectively [56]. Kouloulias et al. in a study for the first implementation of biocompatible balloon between the prostate and the rectum in prostate cancer patients reported acute GI and GU toxicity equivalent to IMRT techniques [57].

Radiotherapy plays also an important role in the management of head & neck cancer, in combination with chemotherapy when indicated. As shown in the metaanalysis by Pignon et al. [58], chemoradiotherapy offers an absolute 4% benefit in 5-year overall survival (OS), with the highest benefit when given concurrently (8% at 5 years) but with increased toxicity [59]. Kouloulias et al. in a recent systematic review reported equivalence of IMRT technique in terms of local control and survival in head & neck cancer patients compared with 2-3D conformal radiotherapy, with a statistically significant reduction in late xerostomia [14]. When it concerns acute toxicity, mucositis and xerostomia, there was only a trend for superiority of IMRT. These results are consistent with the findings of our study; all four patients developed some degree of mucositis, with the majority of them developing grade II mucositis. Acute xerostomia in terms of reduced salivary flow was observed in all four patients in terms of gr I toxicity.

IMRT's main principle of operation is the combination of many segmental beams to produce a complex dose distribution. Because of the numerous factors and procedures that contribute to the IMRT technique there are many sources of uncertainty including basic dosimetry of small fields, treatment planning system (TPS), approximations and limitations in calculation algorithms, the delivery process, multileaf collimator (MLC) positioning accuracy, linearity of the accelerator in the low monitor unit (MU) setting. Above-mentioned aspects impose that the pre-treatment quality assurance (QA) during IMRT is mandatory. Therefore, medical centers that use the IMRT technique also apply a QA protocol, consisting mainly from a quantitative comparison between calculated vs. measured dose distributions. The resulting statistics, such as the percentage dose difference, the distance to agreement (DTA) and the gamma analysis are evaluated according to the defined tolerance limits, set by the centre.

Regarding Quality Control equipment and verification planning, most radiotherapy centers use various dosimetric tools and methods such as radiochromic films, ionisation chambers, thermoluminiscent detectors (TLD's), 2D diode array's, the polymeric gels and Electronic Portal Imaging Devices (EPID) [54]. In spite of that, the previous mentioned tools and methods have advantages and disadvantages for facilitating IMRT QA performance, since most of them are based on

2D techniques, with precision limitations. Additionally, long delays may be experienced during their application, as several processes need to be executed in order to get adequate results. In the recent past, several solutions for volumetric quality assurance, suitable for advanced radiotherapy modes, have been introduced [55]. The Delta^{4PT} pre-treatment system is one of them and recently has been installed in our department, Aretaieion University Hospital Radiotherapy Department.

The DVH evaluation in both anatomical regions of the target volumes and the OARs showed that the Treatment's planning System performance is in good agreement with international guidelines [51]. In prostate cases the gamma statistical analysis performed by Delta^{4PT} software indicated a high accuracy in therapy delivery in comparison to the verification plan data from other centres [60]. When head & neck cases are considered, the gamma index indicated an acceptable performance, higher than 90% conforming to other studies [61]. The lower values of gamma index for the head & neck cases can be attributed to the region complexity and the number of subfields required to be achieved the desirable dose distribution [62].

Conclusions

The first implementation of IMRT for either prostate and head & neck patients in the public sector in Greece, concerning the Aretaieion University Hospital, is evidence now. The IMRT delivery is feasible and effective, although it is a time consuming procedure with a mean treatment time of 25 minutes. Our experience showed that the technique of pre-treatment plan verification using the Delta4^{PT} phantom and its software, provides accurate and reliable results of 3D dose distributions comparisons between the calculated and the deliverable plan. At last but not least, our clinical outcome, in terms of toxicity, is similar with published data in the relevant literature. The dose verification procedure, along with evaluation of late radiation induced toxicity is on-going and further results will be reported with more patients undergoing IMRT irradiation for either prostate or head & neck cases.

References

1. Zelefsky MJ, Levin EJ, Hunt M et al. Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for localized prostate cancer. Int J Radiat Oncol Biol Phys 2008;70:1124-1129.
2. Peeters ST, Heemsbergen WD, Koper PC et al. Dose response in radiotherapy for localized prostate cancer: results of the Dutch multicenter randomized phase III trial comparing 68 Gy of radiotherapy with 78 Gy. J Clin Oncol 2006;24:1900-1906.
3. Al-Mamgani A, van Putten WL, Heemsbergen WD et al. Update of Dutch multicenter dose escalation trial of radiotherapy for localized prostate cancer. Int J Radiat Oncol Biol Phys 2008;72:980-988.
4. Hunt MA, Zelefsky MJ, Wolden S et al. Treatment planning and delivery of intensity-modulated radiation therapy for primary nasopharynx cancer. Int J Radiat Oncol Biol Phys 2001;49:623-632.
5. Liu YM1, Shiau CY, Lee ML et al. The role and strategy of IMRT in radiotherapy of pelvic tumors: Dose escalation and critical organ sparing in prostate cancer. Int J Radiat Oncol Biol Phys 2007;67:1113-1123.
6. Zelefsky MJ, Chan H, Hunt M, Yamada Y, Shippy AM, Amols H. Long term outcome of high dose IMRT for patients with clinically localized prostate cancer. J Urol 2006;176:1415-1419.
7. Michalski JM, Yan Y, Watkins-Bruner D et al. Preliminary analysis of 3D-CRT vs IMRT on the high dose arm of the RTOG 0126 Prostate Cancer Trial: toxicity report. Int J Radiat Oncol Biol Phys 2011;81:S1-S2.
8. Michalski J, Yan Y, Tucker S et al. Dose volume analysis of grade 2+ late GI toxicity on RTOG 0126 after high dose 3DCRT or IMRT. Int J Radiat Oncol Biol Phys 2012;84 (Suppl):14-15.
9. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. J Clin Oncol 2008;26:3770-3776.
10. Hammerlid E, Silander E, Hörnestam L, Sullivan M. Health-related quality of life three years after diagnosis of head and neck cancer—a longitudinal study. Head Neck 2001;23:113-125.
11. Nutting CM, Morden JP, Harrington KJ et al. PARSPORT trial management group. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol 2001;12:127-136.
12. Kam MK, Leung SF, Zee B et al. Prospective randomized study of intensity-modulated radiotherapy on salivary gland function in early-stage nasopharyngeal

carcinoma patients. J Clin Oncol 2007;25:4873-4879.

13. Pow EH, Kwong DL, McMillan AS et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys 2006;66:981-991.
14. Kouloulias V, Thalassinou S, Platoni K et al. The treatment outcome and radiation –induced toxicity for patients with head and neck carcinoma in the IMRT era: a systematic review with dosimetric and clinical parameters. Biomed Res Int 2013;2013:401261. doi: 10.1155/2013/401261
15. Graff P, Lapeyre M, Desandes E et al. Impact of intensity-modulated radiotherapy on health-related quality of life for head and neck cancer patients: matched-pair comparison with conventional radiotherapy. Int J Radiat Oncol Biol Phys 2007;67:1309-1317.
16. Toledano I, Graff P, Serre A et al. Intensity-modulated radiotherapy in head and neck cancer: results of the prospective study GORTEC 2004-03. Radiother Oncol 2012;103:57-62.
17. Gupta T, Agarwal J, Jain S et al. Three-dimensional conformal radiotherapy (3D-CRT) versus intensity modulated radiation therapy (IMRT) in squamous cell carcinoma of the head and neck: a randomized controlled trial. Radiother Oncol 2012;104:343-348.
18. Adams EJ, Convery DJ, Cosgrove VP et al. Clinical implementation of dynamic and step-and-shoot IMRT to treat prostate cancer with high risk of pelvic lymph involvement. Radiother Oncol 2004;70:1-10.
19. Alaei P, Higgins PD, Weaver R, Nguyen N. Comparison of dynamic and step-and-shoot IMRT planning and delivery. Med Dosimetry 2004;29:1-6.
20. Chui CS, Chan MF, Yorke E, Spirou S, Ling CC. Delivery of intensity modulated radiotherapy with a conventional multileaf collimator: Comparison of dynamic and segmental methods. Med Phys 2001;28:2441-2446.
21. Jothybasu KS, Bahl A, Subramani V, Rath GK, Sharma DN, Julka PK. Static versus dynamic intensity modulated radiotherapy: Profile of integral dose in carcinoma of the nasopharynx. J Med Phys 2009; 34:66-72.
22. Kouloulias V. Quality assurance in radiotherapy. Eur J Cancer 2003;39:415-422.
23. Agnew CE, King RB, Hounsell AR, McGarry CK. Implementation of phantom-less IMRT delivery verification using Varian DynaLog files and R/V output. Phys Med Biol 2012;57:6761-6777.
24. Bailey DW, Kumaraswamy L, Bakhtiari M, Malhotra HK, Podgorsak MB. EPID dosimetry for pretreatment quality assurance with two commercial systems. J Appl Clin Med Phys 2012;13:3736. doi: 10.1120/jacmp.v13i4.3736.
25. Oldham M, Thomas A, O'Daniel J et al. A quality assurance method that utilizes 3D dosimetry and facilitates clinical interpretation. Int J Radiat Oncol Biol Phys 2012;84:540-546.
26. Lang S, Reggiori G, Puxeu Vaquee J et al. Pretreatment quality assurance of flattening filter free beams on 224 patients for intensity modulated plans: a multicentric study. Med Phys 2012;39:1351-1356.
27. Low DA, Moran JM, Dempsey JF, Dong L, Oldham M. Dosimetry tools and techniques for IMRT. Med Phys 2011;38:1313-1338.
28. Papoutsaki MV, Maris TG, Pappas E, Papadakis AE, Damilakis J. Dosimetric characteristics of a new polymer gel and their dependence on post-preparation and post-irradiation time: effect on X-ray beam profile measurements. Phys Med 2013;29:453-464.
29. Hauri P1, Verlaan S, Graydon S, Ahnen L, Klöck S, Lang S. Clinical evaluation of an anatomy-based patient specific quality assurance system. J Appl Clin Med Phys 2014;15:4647.
30. Fiorino C, Reni M, Bolognesi A, Bonini A, Cattaneo GM, Calandrino R. Set-up error in supine-positioned patients immobilized with two different modalities during conformal radiotherapy of prostate cancer. Radiother Oncol 1998;49:133-141.
31. International Commission on Radiation Units and Measurements II. Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50), ICRU Report 62. Bethesda, MD; 1999.
32. Kantzou I1, Platoni K, Sandilos P et al. Conventional versus virtual simulation for radiation treatment planning of prostate cancer: final results. J BUON 2011;16:309-315.
33. Kantzou I1, Kelekis N, Platoni K et al. Comparison of conventional and virtual simulation for radiation treatment planning of prostate cancer. J BUON 2010;15:684-689.
34. Garipagaoglu M1, Sengoz M, Senkesen O et al. Does pelvic lymph nodes irradiation using intensity modulated radiation therapy increase rectal and bladder toxicities in patients with prostate carcinoma? JBUON 2010;15:668-673.
35. Kubes J, Dedeckova K, Cvek J et al. Treatment of high risk prostate cancer with combined radiotherapy and hormonal treatment- results and identification of factors influencing outcome. J BUON 2013;18:669-674.
36. Kitamura K, Shirato H, Seppenwoolde Y et al. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. Int J Radiat Oncol Biol Phys 2002;53:1117-1123.
37. Nederveen AJ, Heide UA, Dehnad H, Moorselaar RJA, Hofman P, Lagendijk JJW. Measurements and clinical consequences of prostate motion during a radiotherapy fraction. Int J Radiat Oncol Biol Phys 2002;53:206-214.
38. van Herk M, Remeijer P, Rasch C, Lebesque JV. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000;47:1121-1135.
39. Vanasek J, Odrazka K, Dusek L et al. Experience with intensity-modulated radiotherapy in the treatment of head and neck cancer. J BUON 2013;18:970-976.
40. Zygogianni A, Kyrgias G, Kouvaris J et al. Impact of acute radiation induced toxicity of glutamine ad-

ministration in several hypofractionated irradiation schedules for head and neck carcinoma. Head Neck Oncol 2012;4:86.

41. Grégoire V, Ang K, Budach W et al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines. Radiother Oncol 2014;110:172-181.
42. Anbumani S1, Arunai Nambi Raj N, S Prabhakar G et al. Quantification of uncertainties in conventional plan evaluation methods in Intensity Modulated Radiation Therapy. J BUON 2014;19:297-303.
43. Liu C, Gong G, Zhou T, Wang Y, Yin Y, Li B. The error estimate for contouring the brainstem in radiotherapy of head and neck cancer: a multi-center study from north China. J BUON 2014;19:484-489.
44. Grégoire V, Jeraj R, Lee JA, O'Sullivan B. Radiotherapy for head and neck tumours in 2012 and beyond: conformal, tailored, and adaptive? Lancet Oncol 2012;13:e292-300. doi: 10.1016/S1470-2045(12)70237-1.
45. Feygelman V, Forster K, Opp D, Nilsson G. Evaluation of a biplanar diode array dosimeter for quality assurance of step-and-shoot IMRT. J Appl Clin Med Phys 2009;10:64-78.
46. Sadagopan R, Bencomo JA, Martin RL, Nilsson G, Matzen T, Balter PA. Characterization and clinical evaluation of a novel IMRT quality assurance system. J Appl Clin Med Phys 2009;10:104-119.
47. Marks LB, Yorke ED, Jackson A et al. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys 2010;76:S10-19.
48. Bentzen SM, Constine LS, Deasy JO et al. Quantitative analyses of normal tissues effects in the clinic(QUANTEC): an introduction to the scientific issues. Int J Radiat Oncol Biol Phys 2010;76:S3-9.
49. Li H, Dong L, Zhang L, Yang JN, Gillin MT, Zhu XR. Toward a better understanding of the gamma index: Investigation of parameters with a surface-based distance method. Med Phys 2011;38:6730-6741.
50. Low DA, Harms WB, Mutic S, Purdy JA. A technique for the quantitative evaluation of dose distributions. Med Phys 1998;25:656–661.
51. Ezzell GA, Burmeister JW, Dogan N et al. IMRT commissioning: multiple institution planning and dosimetry comparisons, a report from AAPM Task Group 119. Med Phys 2009;36:5359-5373.
52. Kouloulias VE, Kouvaris JR. Cytoprotective efficacy of amifostine against radiation-induced rectal toxicity: objective and subjective grading scales for radiomucositis. Molecules 2008;13:892-903.
53. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995;31:1341-1346.
54. Van Esch A, Bohsung J, Sorvari P et al. Acceptance tests and quality control (QC) procedures for the clinical implementation of intensity modulated radiotherapy (IMRT) using inverse planning and the sliding window technique: experience from five radiotherapy departments. Radiother Oncol 2002;65:53-70.
55. Anders Gustafsson, 2013. Patient dose calculation based on ScandiDos Delta4PT measurements. http://www.scandidos.com/upload/Documents/References/D001%2032%20013%2001%20White%20Paper%20-%20Delta4DVH%20Anatomy.pdf
56. Peeters ST, Heemesbergen WD, van Putten WL et al. Acute and late complications after radiotherapy for prostate cancer; results of a multicenter randomized trial comparing 68 Gy to 78 Gy. Int J Rad Oncol Biol Phys 2005;61:1019-1034.
57. Kouloulias V, Kalogeropoulos T, Platoni K et al. Feasibility and radiation induced toxicity regarding the first application of transperineal implementation of biocompatible balloon for high dose radiotherapy in patients with prostate carcinoma. Radiat Oncol 2013;8:82. doi: 10.1186/1748-717X-8-82
58. Pignon J-P, le Maitre A, Maillard E, Bourhis J. Metaanalysis of chemotherapy in head and neck cancer (MCH-NC): An update on 93 randomised trials and 17,346 patients. Radiother Oncol 2009;92:4-14.
59. Lee A, Lau W, Tung S et al. Preliminary results of a randomized study on therapeutic gain by concurrent chemotherapy for regionally-advanced nasopharyngeal carcinoma:NPC-9901 trial by the Hong Kong Nasopharyngeal Cancer Study Group. J Clin Oncol 2005;23:6966-6975.
60. Salter BJ, Sarkar V, Wang B, Shukla H, Szegedi M, Rassiah-Szegedi P. Rotational IMRT delivery using a digital linear accelerator in very high dose rate "burst mode". Phys Med Biol 2011;56,1931-1946.
61. Riley S. Patient plan verification with diode arrays. Clatterbridge Center for Oncology NHS Trust Presentation. http://www.scandidos.com/upload/Documents/References/_CCO_Stephen_-_SRPoster.pdf
62. Ezzell G, Galvin JM, Low D et al. Guidance document on delivery, treatment planning, and clinical implementation of IMRT: Report of the IMRT subcommittee of the AAPM radiation therapy committee. Med Phys 2003;30:2089. doi:10.1118/1.1591194)