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Optimization of radiation therapy in non-functioning pituitary adenoma based on temporal lobe dosimetry

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Abstract

Purpose: *To compare the plan quality, normal brain dosimetry and temporal lobe dosimetry of three different radiotherapy techniques- 3field 3DCRT (3F), IMRT and 4- field non-coplanar technique (4FNC) for large irregular non functioning pituitary adenoma (NFPA).*

Materials and Methods: *CT data sets of 28 patients previously treated for NFPA by either a 3F or IMRT (14 patients each) radiotherapy of physicians' choice were utilized to prepare 4FNC to obtain 95% isodose coverage of planning target volume (PTV). GTV previously contoured by CT-MRI fusion was unchanged. The PTV was created by a uniform 3-D expansion of GTV by 5mm margin. Bilateral Temporal lobes were contoured if not done previously. Plan quality was compared by Target coverage, New Conformity Index (NCI) and Homogeneity index (HI). Normal tissue sparing was compared by volume of normal Brain beyond the PTV receiving 80%, 60% and the mean dose, and volume of bilateral temporal lobes receiving the target dose. NCI was calculated using the formula D max /Dp & HI was calculated as D2-D98/Dp x 100.*

Results: *Mean age of the cohort was 36 years with 21 male and 7 female patients. All patients had undergone immobilisation with thermoplast mask with neck flexion or neutral position (16: 12). Twelve patients had undergone 3DCRT with 3F beam arrangement (1: 2-field, 11: 3 field) and 14 had undergone IMRT, non-coplanar beam arrangement being utilized in 14 patients (more commonly with 3DCRT compared to IMRT- 10:4). Two patients had undergone radiotherapy with the 4-field non- coplanar technique. Median volume of PTV was 50cc (range=10 to 185cc). Dose prescription ranged from 45Gy/25 fractions to 54Gy/30 fractions. Mean 95% coverage of PTV by 3F: 4FNC: IMRT was 94%, 95% and 95% respectively. Comparison of mean NCI between 3F, IMRT and 4FNC was 1.08, 1.02 and 1.06 respectively and mean HI between 3F, IMRT and 4FNC was 10.7, 8.84 and 8.9 respectively. Volume of the normal brain beyond the PTV receiving 80%, 60% and 50% of the prescription dose between the 3F, IMRT and 4FNC was D80- 7.88: 4.2: 5.8, D60- 14.5: 7.9: 9 and D50- 18.7: 13: 11. Dose to 13% of right temporal (RT) and left temporal (LT) lobes by 3F, IMRT and 4FNC was RT- 87.8%: 84%: 79% and LT- 89%: 82%: 79%. While it was seen that the target coverage, NCI and HI was superior with IMRT, 4FNC technique while performed in neck flexion position was superior in terms of lesser mean dose to normal brain and dose to bilateral temporal lobes especially in patients with larger PTV's.*

Conclusion: *The four field non coplanar technique provides superior target and normal tissue dosimetry in patients with large PTV non-functioning pituitary adenomas.*

Optimization of radiation therapy in non-functioning pituitary adenoma based on temporal lobe dosimetry.

Introduction

Radiotherapy (RT) forms an important component in the management of non-functioning pituitary adenoma (NFPA). It is indicated for adjuvant therapy for all the patients with NFPA. The technique of RT delivery in NFPA has been evolving over years from a conventionally planned simple three field arrangement to a more complex and high precision radiotherapy to mitigate the late toxicity of radiation. Late toxicity of RT on normal brain and especially temporal lobes which manifests as decline in the neurocognition is well established in a prospective manner, is more pronounced in young adults and is known to affect the quality of life of these patients to a great extent. There is relative paucity of data on prospective comparison of various radiotherapy techniques to look for long term late toxicity, although Volumetric modulated arc therapy (VMAT) has been shown to be superior by dosimetric parameters. Along with this fact, VMAT is not uniformly available at many centres radiotherapy in NFPA is usually performed by 3D Conformal (3DCRT). We compared normal brain and temporal lobe dosimetry of three different radiotherapy techniques for non-functioning pituitary adenoma.

Methodology

Contrast enhanced computed tomography CT data sets of 28 patients previously treated for NFPA either by a 3-field arranged 3DCRT or IMRT (of clinician's preference) with or without non-coplanar beam arrangement to a dose ranging from 45Gy in 25 fractions to 54Gy in 30 fractions was utilized to create a 4-field non-coplanar (4FNC) beam arranged 3DCRT technique. All the patients had undergone immobilisation of the head in neck flexion position to maintain the skull base parallel to the treatment couch. Contrast enhanced CT images were acquired from vertex to sixth cervical vertebra with 3mm spacing. Post Gadolinium enhanced T1 MRI was co-registered with CECT for gross tumour volume (GTV) delineation. A three dimensional isotropic margin of 5mm was given to GTV to create the planning target volume (PTV). Organs at risk (OAR) included normal brain beyond the PTV, optic apparatus and bilateral temporal lobes.

The coordinates of the coplanar 3F, non-coplanar 3F, co-planar IMRT, non-coplanar IMRT and 4FNC are described in the table 1. IMRT plans were all 7 beam arranged co-planar fields or a vertex field (as 7th beam) when the non-coplanar technique was chosen. The GTV which was initially contoured with CECT-MRI co-registration was not modified. PTV was created by uniform 5mm expansion of GTV in a 3D fashion. Bilateral Temporal lobes were contoured if not done previously. Plan quality was compared by Target coverage, New Conformity Index (NCI) and Homogeneity index (HI). Normal tissue sparing was compared by volume of normal Brain beyond the PTV receiving 80%, 60% and the mean dose, and volume of bilateral temporal lobes receiving the target dose. NCI was calculated using the formula D max /Dp & HI was calculated as D2-D98/Dp x 100. Dosimetric parameters of target- Target coverage, Conformity index (CI), Homogeneity index (HI) and OAR dosimetric parameters - D50, D60, D80 of normal brain, D50 and D13 of both the temporal lobes was compared between the three plans. The data was tabulated on SPSS version 21.0 and analysed.

Results

Mean age of the cohort was 36 years with 21 male and 7 female patients. All patients had undergone immobilisation with thermoplast mask with neck flexion or neutral position (16: 12). Twelve patients had undergone 3DCRT with 3F beam arrangement (1: 2-field, 11: 3 field) and 14 had undergone IMRT, non-coplanar beam arrangement being utilized in 14 patients (more commonly with 3DCRT compared to IMRT- 10:4). Two patients had undergone radiotherapy with the 4-field non- coplanar technique.

Median volume of PTV was 50cc (range=10 to 185cc). Dose prescription ranged from 45Gy/25 fractions to 54Gy/30 fractions. Mean 95%

coverage of PTV by 3F: 4FNC: IMRT was 94%, 95% and 95% respectively. Comparison of mean NCI between 3F, IMRT and 4FNC was 1.08, 1.02 and 1.06 respectively and mean HI between 3F, IMRT and 4FNC was 10.7, 8.84 and 8.9 respectively. Volume of the normal brain beyond the PTV receiving 80%, 60% and 50% of the prescription dose between the 3F, IMRT and 4FNC was D80- 7.88: 4.2: 5.8, D60- 14.5: 7.9: 9 and D50- 18.7: 13: 11. Dose to 13% of right temporal (RT) and left temporal (LT) lobes by 3F, IMRT and 4FNC was RT- 87.8%: 84%: 79% and LT- 89%: 82%: 79%. While it was seen that the target coverage, NCI and HI was superior with IMRT, 4FNC technique while performed in neck flexion position was superior in terms of lesser mean dose to normal brain and dose to bilateral temporal lobes especially in patients with larger PTV's.

The co-ordinates of all the plans are explained in the table 1 and depicted in Figure 1. The cumulative DVH of all the three plans in a case example is shown in Figure 2. Temporal lobe dosimetry as a percentage of prescription doses are shown in Figure 3. Comparison of dosimetric parameters of target, normal brain D50, D60 and D80 and the temporal lobe dosimetry is shown in table 2 and depicted in Figure 4.

Target coverage to 95% of the PTV and mean CI was superior with increase in number of beams by IMRT compared to 4FNC and 3F. Mean HI with lower by 3F, while it was comparable between IMRT and 4FNC. Mean dose to normal beyond the PTV was higher with IMRT compared to 3DCRT plans, which could possibly be explained by more number of beams. D60 was comparable between 3F and 4FNC. D80 was least with 4FNC.

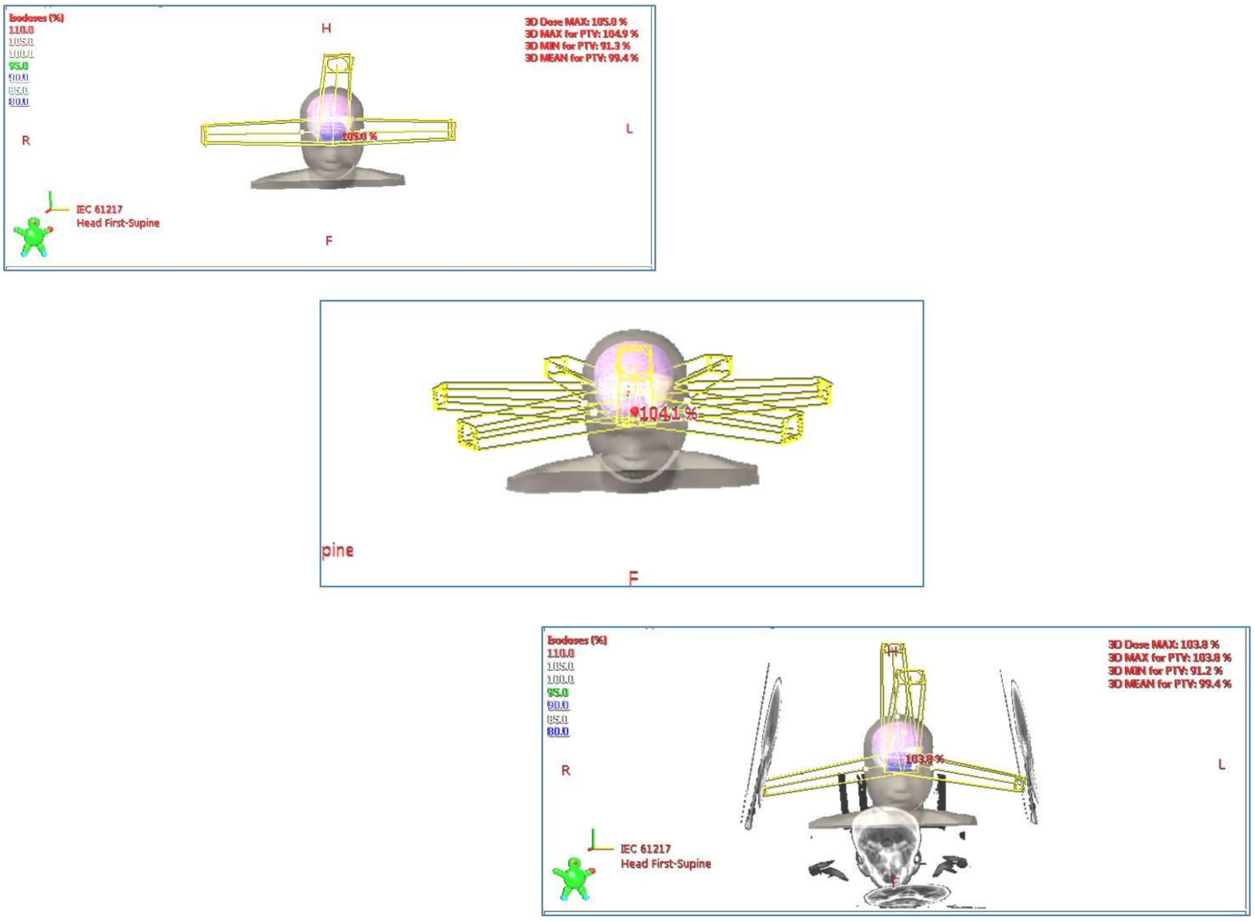

Figure 1- Beam arrangements

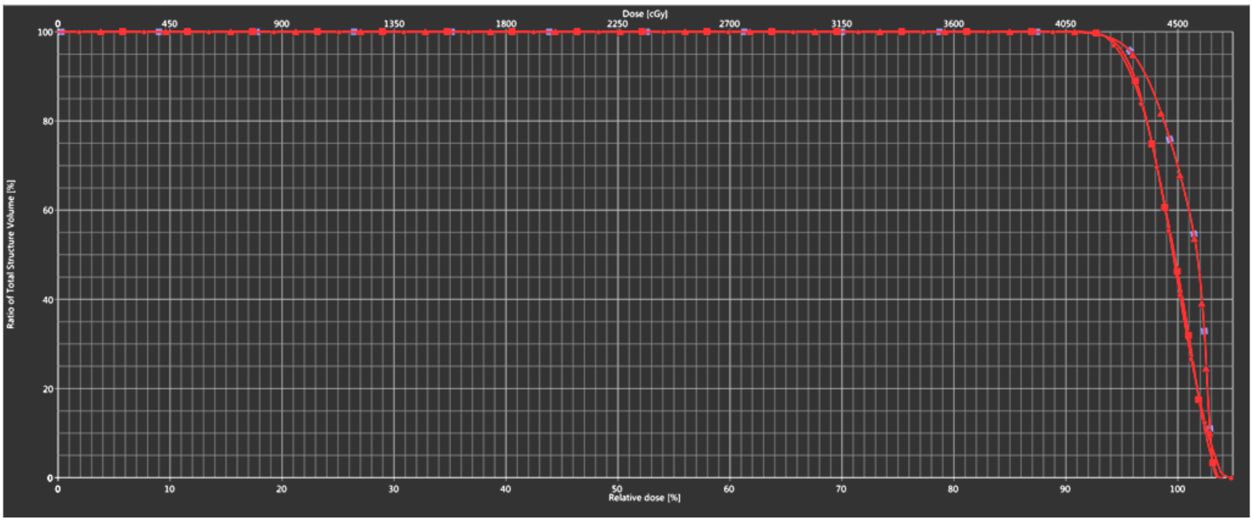

Figure 2 Cumulative DVH of all the three plans in one case example

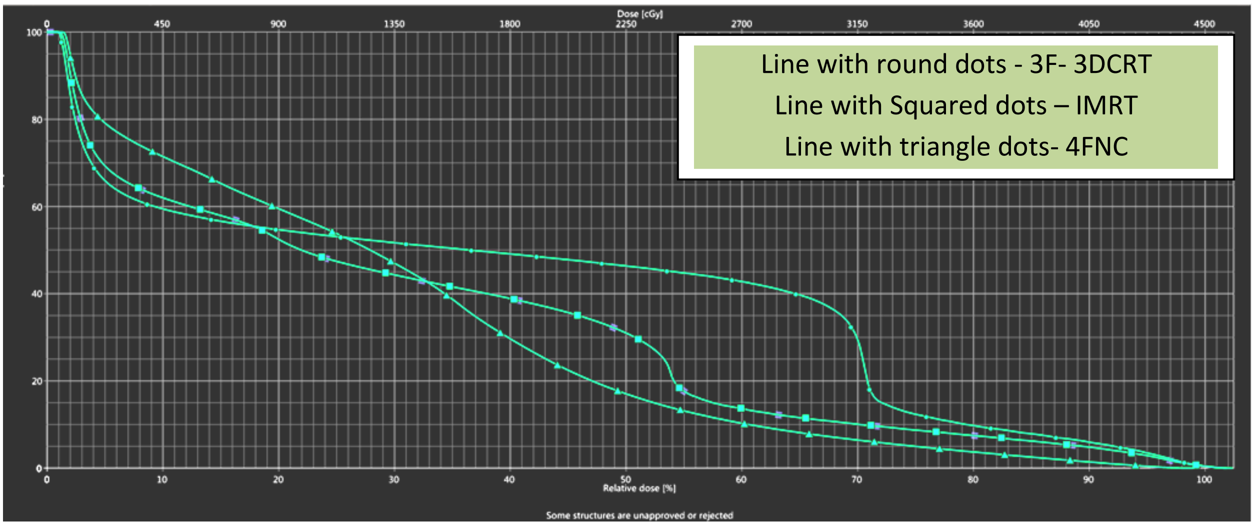

Figure 3 Temporal brain dosimetry- % of temporal brain receiving the prescription isodose

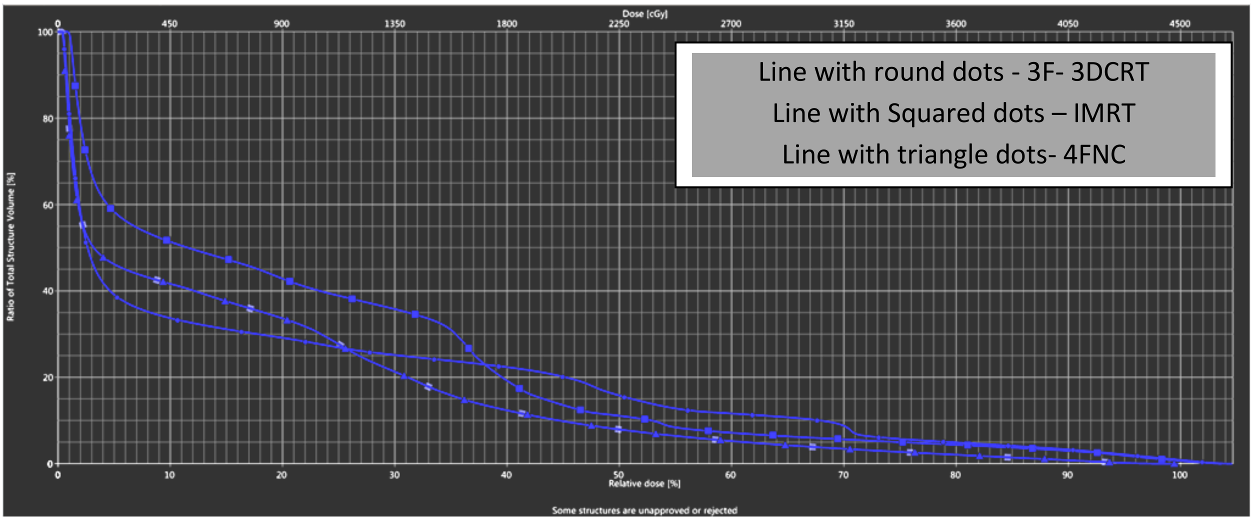

Figure 4 Normal brain DVH- the D80, D60 and Mean dose of normal Brain from various plans

Table 1: Beam arrangements and table co-ordinates

Field 1- Beam arrangements				
Field arrangement	**Coplanar/ Non-coplanar**	**Gantry**	**Couch**	**No of patients**
2-field	Coplanar	90	0	1
		270	0	
3- field	Coplanar	90	0	3
		270	0	
		40	0	
3- field	Non-coplanar	90	0	8
		270	0	
		40	90	
4- field	Non-coplanar	100	350	2
		260	10	
		40	90	
		110	90	
IMRT	Coplanar	51	0	4
		102	0	
		153	0	
		204	0	
		255	0	
		306	0	
		357	0	
IMRT	Non-Coplanar	51	0	10
		102	0	
		153	0	
		204	0	
		255	0	
		306	0	
		40	90	

Table 2: Target and normal brain volumes and dosimetry parameters

PTV median (range)	Brain – PTV median (range)	NCI median (range)		HI median (range)		Normal brain dosimetry				
53.5 cc (10-185cc)	1216 cc (989-1498 cc)	NCI= D max/Dp		HI=D2-D98/Dpx100			D50	D60	D80	Temporal (% of Dp)
		3F	1.08	3F	10.7	3F	18.68	14.56	7.88	89%
		IMRT	1.02	IMRT	8.84	IMRT	12.9	7.91	4.2	83%
		4FNC	1.06	4FNC	8.9	4FNC	11.28	9.12	5.8	79%

Discussion

The current standard of care for pituitary radiotherapy remains three dimensional conformal radiotherapy(12) and that IMRT, for the most part, offers no advantage in comparison with standard CRT for the majority of patients with sellar and suprasellar tumours. Radiotherapy gives long-term tumour control up to 94% of patients at 10 years and 88% at 20 years(1) and with technical improvement, treating less normal brain to high radiation doses with conformal radiotherapy to reduce late radiation toxicity is the norm(6). Doses of 45 Gy are found to give equal local tumour control rates similar to doses of 50 Gy and higher(5). Individual fraction doses above 1.8 Gy and total doses above 45 Gy are independent risk factors for Radiation induced Hypopituitarism(8). Employing a higher number of radiation beams can be detrimental, as increasing the number of radiation beams leads to larger volumes of normal brain receiving low radiation doses(4).

It is understandable that registration of CT and MRI images for better volume delineation and planning, itself may reduce the volume of normal brain being irradiated, IMRT may have very limited benefit over a good 3D- conformal plan apart from very few instances where the tumour may be large, irregular and located very close to a critical structure[7]. Although arc based IMRT techniques have demonstrated dosimetric superiority compared to other conformal techniques, it is not uniformly available in many centres. Apart from dosimetric advantages, factors such as ease of implementation, quality assurance requirements, and time-resource burden also need to be considered when selecting the appropriate conformal technique[9]. The immobilisation methods utilized for the treatment of pituitary adenomas have ranged from stereotactic frames, specialized firm mask to a three point conventional thermoplastic mask with a relocation accuracy of 5mm. With availability of planar and volumetric imaging facility for verification, it is feasible to use a simpler immobilisation device which is comfortable and less labor intensive[11].

Brada et.al described a non coplanar technique by increasing the number of spatially separated, conformally fixed beams to reduce the degree of sparing the normal brain with ease of application for everyday use[2]. Four non opposing non coplanar fields were used to reduce the dose to both the temporal and frontal lobes, achieving considerable sparing of normal brain in the 80% and 60% dose regions and demonstrated that 4 four static, conformal, noncoplanar beams provide an acceptable, practical and adaptable class solution for SCRT of sellar tumours both in terms of normal tissue sparing and feasibility within the routine clinical practice.

Patients with PA suffer from mood disturbances, cognitive impairments, and difficulties in memory and executive functions[13]. Additionally, accelerated cognitive decline may develop over many years following RT. The incidence and severity of this complication is dependent on radiation fraction dose, total dose, and volume[14]. The temporal lobe is crucial for acquisition of new information as well as its storage and retrieval, which seems to decrease after RT. High dose irradiation volumes in the temporal and frontal lobes with conventional radiotherapy technique has been also widely believed to cause late neurocognitive dysfunction[3]. Jalali et.al have found dose- volume correlation of temporal lobe damage with doses more than 43.2 Gy to 13% of the left temporal lobe causing higher neuro-cognitive decline even in adults[10]. They observed that a smaller target and reduction of margins may have potential reduction in temporal lobe volumes receiving higher doses and reducing risk of cognitive damage.

Our study was aimed at integrating these concepts- to create a 4-field non coplanar plan to patients, predominantly young with irregular target volumes and compare the dosimetric superiority of this to a 3 field technique and an IMRT plan, in terms of normal temporal lobe doses. The 4 field technique had target coverage and conformity comparable to the IMRT plans. Increase in number of beams for an IMRT plan to improve target coverage and homogeneity led to increase in doses of normal brain receiving mean dose, 60% and 80% doses. The 4 field plan demonstrated dosimetric superiority in terms of better target coverage, and superior normal brain sparing especially the temporal lobes compared to a 3 field 3DCRT. In patients with larger PTV, mean doses to normal brain by 4FNC and IMRT was comparable.

Conclusion

The four field non-coplanar radiotherapy technique demonstrates superior normal brain and temporal lobe sparing compared to IMRT with comparable target volume coverage and conformity.

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