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Comparison of helical tomotherapy and mixed beam treatment plans for superficial head and neck cancers

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COMPARISON OF HELICAL TOMOTHERAPY AND MIXED BEAM TREATMENT PLANS FOR SUPERFICIAL HEAD AND NECK CANCERS

A Thesis

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Abstract

Purpose: To compare helical tomotherapy (HT) with mixed beam therapy (electron and IMRT) plans for superficial parotid gland and nasal cavity tumors.

Methods: Mixed beam and HT dose plans were developed for five patients with superficial tumors (planning target volume or PTV < 5.5 cm depth), three with parotid gland tumors and two with nasal cavity tumors. Seven mixed beam plans included a 5 or 7-field photon IMRT plan optimized on top of a single en-face 16 or 20 MeV electron beam dose distribution. The ratio of photon to electron beam weights (at depth R_{100}) were 1:0 (IMRT only), 2:1, 1:1, 1:2, 1:3, 1:4, and 0:1 (electrons only). Planning objectives for HT plans were set as closely as possible to those in the mixed beam plans, and were determined using our clinical planning protocol for head and neck cancers. The resulting dose distribution from each plan was evaluated using dose-volume quantities, tumor control probability (TCP), normal tissue complication probability (NTCP), and a clinical evaluation by a radiation oncologist.

Results: In general, the HT plans showed better target coverage and dose homogeneity index (DHI) than the mixed beam plans. For the parotid patients, the DHI improved an average of 0.056 and 0.035 for the nasal cavity patients compared to the mixed beam plan. TCP was comparable in all patients. NTCP for the mixed beam plan was generally lower or comparable to HT with the largest improvements seen in the contralateral parotid, eye, and lens. Also, the mixed beam plans yielded more favorable PTV and normal tissue results for a single shallow uniform PTV using a heavier weighted electron to IMRT ratio (1:3 or 1:4 ratio of electron to IMRT).

Conclusions: The study showed that while HT plans had better target coverage and dose homogeneity, the mixed beam plans (electron and IMRT) had comparable tumor control probability and have the potential for improving NTCP for distal normal tissue for superficial uniform PTVs.

Chapter 1 Introduction

1.1 Head and Neck Cancers Overview

Head and neck cancers comprise a large group of malignant tumors that account for roughly 6 percent of all malignancies in the United States. The annual incidence for head and neck cancers according to the Surveillance, Epidemiology, and End Results (SEER) program is 25 per 100,000 in the United States (www.cancer.org, 2009). Often head and neck cancers are treated with radiation therapy either in conjunction with surgery or as the primary treatment. Over the last several decades, advances in radiation therapy delivery technology have lead to new treatment techniques that have enabled clinics to treat more patients definitively, better spare organs at risk, and generally improve the quality of life for patients following treatment. This general progression of treatment techniques is now described.

1.1.1 Treatment Techniques

Superficial head and neck cancers have for many years been treated with electron beams, often mixed with photons (Tapley, 1976; Vaeth, 1968). The electron and photon energies and the amount of dose delivered by each were determined based on the maximum depth of the lesion to be treated. The advantage of the electron beams is that the distal dose distribution rapidly falls off. Superficial planning target volumes, PTVs, especially those with distal critical structures, take advantage of this fall off (Hogstrom, 2003). Because electron beams have no exit dose (besides bremsstahlung) past the practical range (R_p), they are particularly useful when treating unilateral targets, within 6 cm of the surface, that require a low dose to contralateral tissues such as nose, parotid, ear, oral cavity, and oropharynx (Perez, 2004). The photon component of the mixed beam helps spare the skin at the surface and increases the depth that can be treated. However, these treatments have limitations. They often treat large volumes of normal tissue to high doses in order to obtain the desired dose to the irregularly shaped planning target volume; this sometimes required to abut fields which lead to dose inhomogeneity. Also, irregular

surfaces and internal heterogeneities can lead to increased dose heterogeneities, i.e. hot and cold spots (Hogstrom, 2003). These conventional techniques have been further improved on by IMRT.

1.1.1.1 Intensity Modulated Radiation Therapy (X-rays)

Intensity modulated radiation therapy (IMRT) with x-rays is a type of radiation therapy that uses computer-generated images to conform and match the radiation to the size and shape of a tumor. With IMRT, the radiation beam is subdivided into small beamlets of radiation that enter the body from many different angles and intersect the tumor in such a way that the total radiation dose can avoid normal tissues and create concave shapes.

Over the years, intensity modulated delivery techniques have been shown to improve dose distributions compared to electron and conventional mixed techniques. Intensity-modulated radiotherapy (IMRT) in many cases can be substituted for a treatment in which external beam radiation is an appropriate choice. Cozzi *et al.* (2001) found that IMRT was superior to conventional non-optimized mixed beam treatments in target coverage and organs at risk (OAR) involvement in five advanced cancer head and neck cases. The mean conformity index value (the ratio between treated volume at 90% dose level and PTV) for the five advanced head and neck tumors were 1.93 for mixed beam and 1.60 for IMRT. The IMRT provided an advantage over the conventional mixed beam plans through increased target coverage and avoiding the spinal cord in their deeper advanced head and neck cancers.

The main difference between conventional static mixed beam treatments and IMRT is that the latter provides an extra degree of freedom (the intensity modulation, usually through multi-leaf collimators) and is able to conform well to PTVs that require steep dose gradients (Khan, 2003). Because of the intensity modulation, highly conformal dose distributions can be delivered. This leads to plans in which the dose to the PTV can be increased, while at the same time decreasing the maximum dose to the surrounding healthy tissue (Ezzell *et al.*, 2003; Galvin *et al.*, 2004). In most cases the result is better tumor control and lower normal tissue complication probabilities. The previous studies compared static beam IMRT. Another means of delivering IMRT is helical tomotherapy.

1.1.1.2 Helical Tomotherapy

Helical tomotherapy is an advanced type of IMRT, first developed by TomoTherapy Inc. (Madison, WI). The TomoTherapy Hi-Art System uses a technique where the patient is treated by a rotating gantry with a linear accelerator head. The patient is translated through the 85 cm wide diameter bore as seen in (Figure 1), much in the same manner as a helical CT machine. The Hi-Art system uses a 6 MV fan beam, collimated by a binary multi-leaf collimator, to deliver a helical intensity-modulated radiation beam (Mackie *et al.*, 1993). The binary multi-leaf collimator consists of 64 leaves which can be opened to project beamlets at 51 distinct angles for each rotation. Therefore, in a single rotation around the patient, the binary multi-leaf collimator is able to produce 3264 possible beamlets. When all the leaves on the multi-leaf collimator are retracted, the maximum field width is 40 cm at the axis of rotation. The theoretical advantage of helical tomotherapy is that the large number of potential beamlets will improve the adjustability of the dose distribution.

While relatively new, TomoTherapy is a treatment modality that has come into use for the treatment of numerous disease sites. Previous works have examined helical tomotherapy (HT) and generally conclude that HT is capable of delivering dose distributions that are equivalent to or better than distributions delivered with fixed-beam IMRT. Lee *et al.* (2008) found that HT significantly improved target dose uniformity and target coverage for parotid tumors compared with fixed-beam IMRT. HT has also been compared to mixed beam techniques, that is electron beams combined with photon beams, in the chest wall (Ashenafi, 2006) and found HT to be an attractive alternative in post-mastectomy chest wall with supraclavicular fields due to the maintaining a uniform dose distribution to the PTV while sparing normal tissue (e. g. ipsilateral lung in this case). Also, HT has been shown suitable for disease sites historically treated with electrons. For total scalp, Orton *et al*. (2005) showed that tomotherapy plans had more homogeneous target dose and improved critical structure dose when compared to state-of-the-art linac techniques. Target equivalent uniform dose (EUD) for the best tomotherapy plan was slightly higher than for the conventional plan, while the volume of brain tissue receiving over 30 Gy was reduced

by two thirds (Orton *et al.*, 2005). For medulloblastoma, Penagaricano *et al*. (2009) showed that craniospinal axis irradiation using HT yielded encouraging patient outcomes and acute toxicity profiles. The increased conformity is most likely attributable to the large number of intensity modulated fields delivered and to having a rotating radiation source synced with treatment couch movement to avoid abutting individual fields.

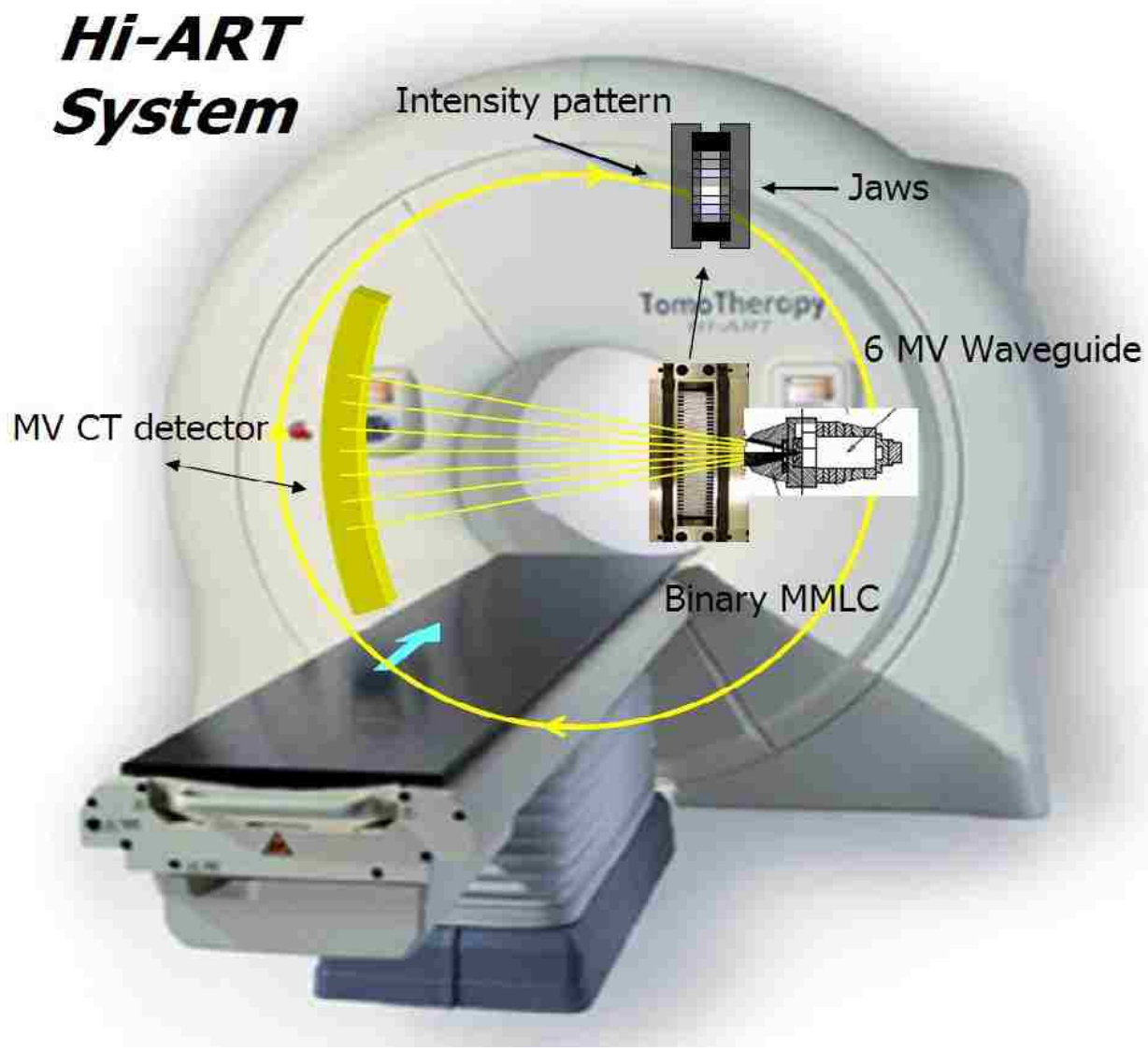

Figure 1 A Helical Tomotherapy treatment machine is shown rotating as the couch passes through the bore of the gantry (Mackie *et al.*, 2003).

1.1.1.3 Intensity Modulated Radiation Therapy with Electrons

Despite the advantages of HT, there remains a potential benefit of using electrons, especially for superficial targets. One such benefit is the finite range of the electron. Electrons could reduce the overall integral dose delivered to the healthy tissue. IMRT treatments often treat large volumes to low doses because of the numerous beam angles. This could be problematic to long term survivors who could be at risk of secondary radiation-induced tumors.

Several research groups have investigated the combination of IMRT with electrons. Chan *et al.*, (2006a) at Memorial Sloan-Kettering Cancer Center investigated the feasibility of combining electrons with IMRT for patients with extensive scalp lesions. They found that mixing IMRT with electrons reduced the dose to the brain with the same dose conformity and homogeneity as the conventional plan in the PTV. They suggested that IMRT with electrons is a viable treatment modality for these scalp lesions. Chan *et al.*, (2006b) also compared IMRT mixed with electrons and IMRT alone for malignant pleural mesothelioma and found that while both techniques provided excellent target coverage and normal tissue sparing, the addition of the electron beams improved the sparing critical structures.

Mu *et al.* (2004) compared IMRT with mixed beam (IMRT plus electrons) plans that were manually optimized for various deep-seated tumors in the head and neck, and concluded that both methods produced clinically acceptable plans. However, the integral dose outside the PTV was generally lower with the mixed beam plans compared to IMRT plans. However, this study examined only deep-seated target volumes in the head and neck region, and the mixed beam plan optimized by a manual iterative process.

The results of preliminary studies (Surucu, 2009) have indicated that it may be possible to utilize the finite range of electrons (a modality available from most linear accelerators) to spare adjacent critical structures, while at the same utilizing the highly conformal doses of IMRT to improve dose inhomogeneities in the PTV. What was unknown was how HT, a technique with some advantages over

conventional IMRT, would compare to a mixed beam technique that utilized conventional IMRT and electrons.

1.2 Parotid and Nasal Cavity Tumors

Two disease sites would make interesting candidates for a comparison of HT and IMRT mixed with electrons due to their superficial locations: Parotid gland tumors and nasal cavity tumors. Irradiation of parotid gland tumors can lead to complications from the many critical structures nearby. One such serious late complication is xerostomia (dryness of the mouth), which can reduce the quality of the life for the patient. Another is myelitis and necrosis of the spinal cord, which may lead to paralysis. Nasal cavity tumors are also challenging to treat because of the brainstem, optic chiasm, retinas, lenses, and brain. Both of these locations are superficial enough to take advantage of the electron's depth dose curve.

Carcinomas of both the parotid gland and nasal cavity are rare. According to the annual SEER Cancer Statistics Review (www.Cancer.org, 2009), 6000 parotid gland and 2000 nasal cavity tumors are diagnosed each year in the United States. Because of the proximity to critical adjacent sensitive structures in the head and neck, the management of these malignancies has been challenging. For all nasal cavity or paranasal sinus cancers combined, the relative 5-year survival (which is a way of comparing survival of people who have the specific disease with those who do not) is 54%. Survival tends to worsen as the stage increases -- for stage 1 disease, the 5-year relative survival is 83%, but for stage IV disease it is only 25%. The outlook is slightly better for salivary gland cancers. For stage 1 the relative 5-year survival rate is 96%, but for stage IV it is only 37% (www.cancer.org, 2009). There is a need to indentify treatment approaches that improves these outcomes.

1.3 Statement of the Problem

Previously studies have compared

- HT to conventional mixed beams in post-mastectomy chest wall (Ashenafi, 2006)
- HT to IMRT in parotids (Lee *et al.*, 2008)

- HT to mixed beam for total scalp (Orton *et al.*, 2005; Chan *et al.*, 2006b)
- HT to conventional mixed beam for craniospinal (Penagaricano *et al.*, 2009)

General conclusions from these studies are that HT is suitable and in many ways superior for a variety of head and neck cases and that IMRT mixed with electrons could offer some potential advantages over IMRT only plans. However, no published studies to date have compared helical tomotherapy to advanced mixed beam techniques (IMRT in conjunction with electrons) for superficial head and neck targets. Moreover there is general lack of guidance in the literature for constructing IMRT-electron plans for superficial targets.

1.4 Hypothesis/Specific Aims

The hypothesis of the current study is that for select superficial head and neck cancers that helical tomotherapy can plan improved dose homogeneity with equal or better normal tissue sparing than plans that optimize a static IMRT field on top of a single unmodulated electron beam.

Aim 1: Generate a database of patients previously treated at our institution from superficial head and neck cancers.

- Search previously treated patients with Pinnacle treatment plans for superficial head and neck tumors. The study will focus on, but not limited to, malignant paranasal and parotid tumors with planning target volumes (PTVs) less than 5.5 cm from the surface. The primary diagnosis groups to be searched will be major salivary glands, nasal cavity, maxillary sinus, and nose.
- After the appropriate patients are selected, sensitive data specific to each patient will be anonymized and placed into a Health Insurance Portability and Accountability Act (HIPAA) compliant database.

Aim 2: Develop HT and mixed beam plans that best meet the treatment prescription.

- Plan each HT treatment on the TomoTherapy Hi-Art planning system.

- Plan each mixed beam treatment on the Pinnacle treatment planning system by optimizing a IMRT plan on top of an electron dose distribution.

Aim 3: Evaluate and compare each plan based on *clinical*, *dosimetric*, and *biological* endpoints.

- For the *clinical* comparison, an American Board Radiology certified radiation oncologist will review the HT and mixed beam plans and evaluate each using a multiple choice questionnaire focusing on the clinical acceptability of each plan, reasons why a plan was preferred, and how the HT plan compared to the mixed beam plan.
- Compare metrics for *dosimetric* comparison, including dose volume histograms (DVHs) for involved structures, the conformity index, dose homogeneity index, the volume of normal tissues receiving low doses, and the minimum, maximum and mean dose to the planning target volumes (PTVs) and organs at risk (OARs).
- The *biological* evaluation will include a comparison of calculated tumor control probability and the normal tissue complication probability for both plans.

Chapter 2 Materials and Methods

2.1 Aim 1: Patient Database - Generate a Database of Patients Previously Treated at our Institution for Superficial Head and Neck Cancers

2.1.1 Patient Selection Criteria

Five patients with superficial head and neck cancers were selected for comparison of helical tomotherapy and advanced mixed beam (IMRT with electrons) plans. Mary Bird Perkins Cancer Center (MBPCC) has maintained a computer archive of patient treatment plans since August 2000. This database was searched for superficial head and neck cancers. The criteria for selecting patients for the study were 1) that the primary PTV did not extend medially beyond the therapeutic range of a 20 MeV electron beam, which is approximately 5.5 cm in tissue, and 2) that CT scan data was readily available from a separate archive maintained by on-site CT technologists. The CT scan data can be quickly exported from the CT machine to the TomoTherapy workstation however, exporting from the Pinnacle workstation to TomoTherapy is tedious and time consuming thus the reason for requiring readily available CT scan data.

The clinical record and verify system (Mosaiq, IMPAC Medical Systems, Sunnyvale, California) maintains a database of patients treated at MBPCC. The print report function was used to query the database for two primary diagnosis groups: 160.0 (nasal cavity/middle ear/auxiliary sinus) and 142.0 (major salivary glands). Of the primary diagnosis groups searched, 81 patients for nasal cavity and 77 major salivary gland (parotid gland) patients were returned. 6 nasal cavity and 8 major salivary glands met the criteria. From these, 2 nasal patients and 3 parotid patients were chosen. PTVs with highly non-uniform depth were rejected in order to use a single energy electron field and avoid abutment issues. Table 1 indicates the patients' diagnosis and staging (if applicable) location of the disease, sex, and approximate age at initial consultation.

Table 1 Relevant disease data for patients selected in the study

Patient	Diagnosis	Staging	Disease location	Sex	Age
1	Intermediate grade mucoepidermoid carcinoma	T1N0M0	Right parotid	F	53
2	Squamous cell carcinoma	Unstaged	Left parotid	M	80
3	High grade adenoidcystic carcinoma	Unstaged	Right parotid	F	36
4	Moderately differentiated squamous cell carcinoma	T1-2N0M0	Left nasal septum	M	73
5	Squamous cell carcinoma	cT1N0M0	Left nasal septum	F	90

2.1.2 Anonymization and Patient Data Import

The original Pinnacle treatment plans were restored from archived tape or disc to the research Pinnacle workstation for mixed beam planning. During this process, the patient name and medical record number were removed from the treatment plan and CT data set. Both the *.header, *.ImageSet, and patient file were modified. The patient's name and medical record number were then replaced with a numeric code which is linked to a master list of patients used for research and maintained by the project director. This was done to maintain patient confidentiality in accordance with Mary Bird Perkins Cancer Center's HIPPA protocol.

Along with the restored Pinnacle plans, CT data were sent directly from the CT scanner (GE Discovery ST or Lightspeed) to the TomoTherapy planning station for HT planning. The original 512 x 512 datasets were resampled to 256 x 256, and unnecessary CT slices were cut from the dataset in order to improve optimization and dose computation time.

2.2 Aim 2: Treatment Plans - Develop HT and Mixed Beam Plans that Best Meet the Treatment Prescription

All mixed beam plans were constructed using the Philips Pinnacle^3 (Philips Medical Systems, Bothell, WA) treatment planning system (version 8.1x). Helical tomotherapy plans were constructed using TomoTherapy Hi-Art treatment planning system (version 3.1.2). Contours, planning methods, and optimization methods are described below.

2.2.1 Contours

PTVs contours were generated by a physician in the original archived plans. Volumes for the primary PTV were 355.4 cm^3, 197.7 cm^3, and 353.6 cm^3 for parotid patients 1, 2, and 3 respectively; and 57.6 cm^3, 28.69 cm^3 for nasal cavity patients 4 and 5.

Most organs at risk (OARs) were generated by either the physician or the dosimetrist (evaluated and modified by the physician if necessary) in the original plan. The OARs previously contoured for the parotid patients were the contralateral parotid, eyes, lenses, optic nerve, and spinal cord. For some of the patients, the physician contoured additional regions of interest based on the patient's previous medical history, and PTV location. The auxiliary OARs were fifth cranial nerve, optic chiasm, auditory system, lips, and brain. The OARs previously contoured for the nasal cavity patients were the spinal cord, eyes, lenses, and optic nerves.

2.2.2 Bolus

For the parotid gland tumors, in order to provide a build-up of dose to the PTV near the skin surface or to surgical scars in these post-operative patients, a tissue-equivalent bolus was contoured. The bolus also served to compensate for missing tissue, around the ear. Without the bolus, the electron dose contributions would be highly inhomogeneous due to a lack of scatter equilibrium, causing a decrease of dose in the shadow of a protrusion and an increase in dose around its periphery (Hogstrom and Almond,

2006). The bolus for the parotid patients was either contoured as a 0.5 cm or 1.0 cm thick (depending on the depth of PTV, energy of electron beam, and OAR distal to the PTV) expansion to the skin, as seen in Figure 2.

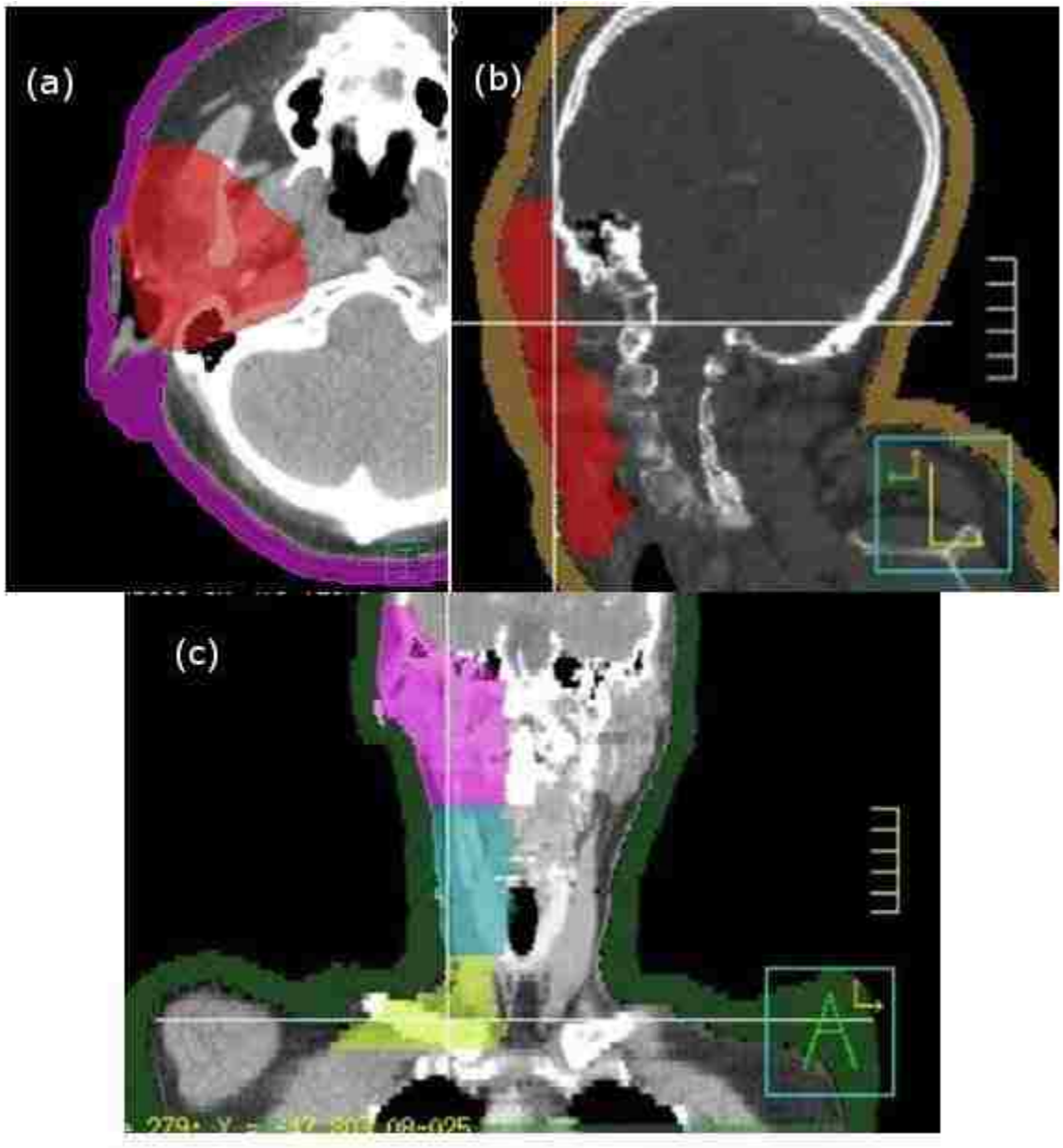

Figure 2. A Transverse and sagittal views through the PTV of patient 1(a), patient 2 (b), and patient 3 (c). Water equivalent bolus of 0.5 cm (a) or 1.0 cm (b and c) thickness is placed over the patient's skin. The PTVs for the patients can be seen color contoured inside the skin and the bolus contoured outside.

For the nasal cavity patients, in order to provide tissue compensation around the nose, a tissue-equivalent bolus was contoured. The bolus was contoured over the nose (about 0.5 cm thick at the apex of the nose) for patient 4 and was scanned in during CT for patient 5 (as seen in Figure 3 (b)). In order to prevent any sharp edges in the electron field, the bolus was extended in a mushroom shape over the skin collimation on the eyes (as seen in Figure 3 (a)). A 1.0 cm thick lead equivalent skin collimation was contoured over the eyes to shield the lenses.

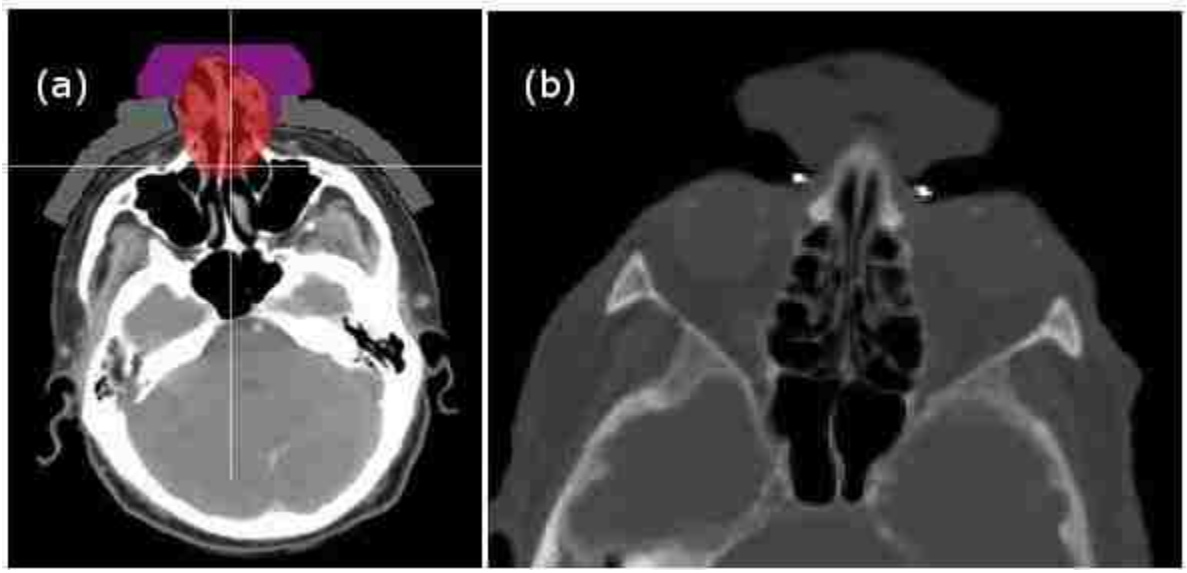

Figure 3. Boluses for nasal cavity patients are shown. On the left is patient 4 (a) that has a hand contoured water equivalent bolus seen in purple with a 1.0 cm lead equivalent skin collimation seen in gray. On the right is patient 5 (b) with the CT scanned bolus on the patient before the lead skin collimation was added.

All contours were generated using the Pinnacle treatment planning system and copied to the Hi-Art planning system for HT planning and optimization. It should be noted that the optimization algorithms for the two systems differ in the treatment of overlapping contours (an example would be the contour for the lens of the eye overlapping with the contour of the eye). The Pinnacle planning system optimizes for any voxels that overlap as if they belonged to both structures. On the other hand, for structures within a particular class (i.e., PTVs or OARs), the TomoTherapy planning system uses a user-designated priority system to determine which structure an overlapping voxel belongs, and used the

corresponding dose constraint for that structure. For the patients in this study, the only OAR structure overlaps were the lens with the eyes in the HT plans and the lens were given priority.

2.2.3 Dose Limiting Structures

For IMRT plans, higher than desired dose levels are sometimes produced in regions outside the PTV and OAR contours. For these cases, dose limiting structures may be used to contain dose. Dose limiting structures are used in inverse-planning methods such as HT and IMRT plans. They are contoured in such a way that the dose distribution is constrained not to exceed a certain limit. An example of a commonly used dose limiting structure is a ring. A ring normally surrounds the PTV as seen below in Figure 4. By using a dose-shaping structure such as a ring, the optimization routine will reduce peripheral hot spots and require similar dose contributions from each beam. For these cases a ring was created by a 3 step process. 1) An ROI was created by radially expanding the PTV by 1.0 cm. 2) A second ROI was created by radially expanding the PTV by 1.5 cm. 3) A final ROI called "ring" was created which uses the larger (1.5 cm PTV expansion) ROI as the source and then avoid the interior of the smaller (1.0 cm PTV expansion) ROI. The ring ROI was used for all mixed beam plans. HT plans did not require a ring because a high modulation factor was not chosen.

For the IMRT planning component of the mixed beam plans, a hot spot would occasionally occur outside of the PTV but not in an OAR. In those cases, a "hot spot" contour was drawn around the area of increased dose and then used again in the optimization process to reduce the dose in that area. Hot spot contours were not needed on the TomoTherapy plans.

2.2.4 Plan Parameters

Once all the contours and dose limiting structures were defined, pre-optimization plan parameters values were set. Table 2 and 3 show a summary of the plan parameters values used for the HT and mixed beam plans, respectively.

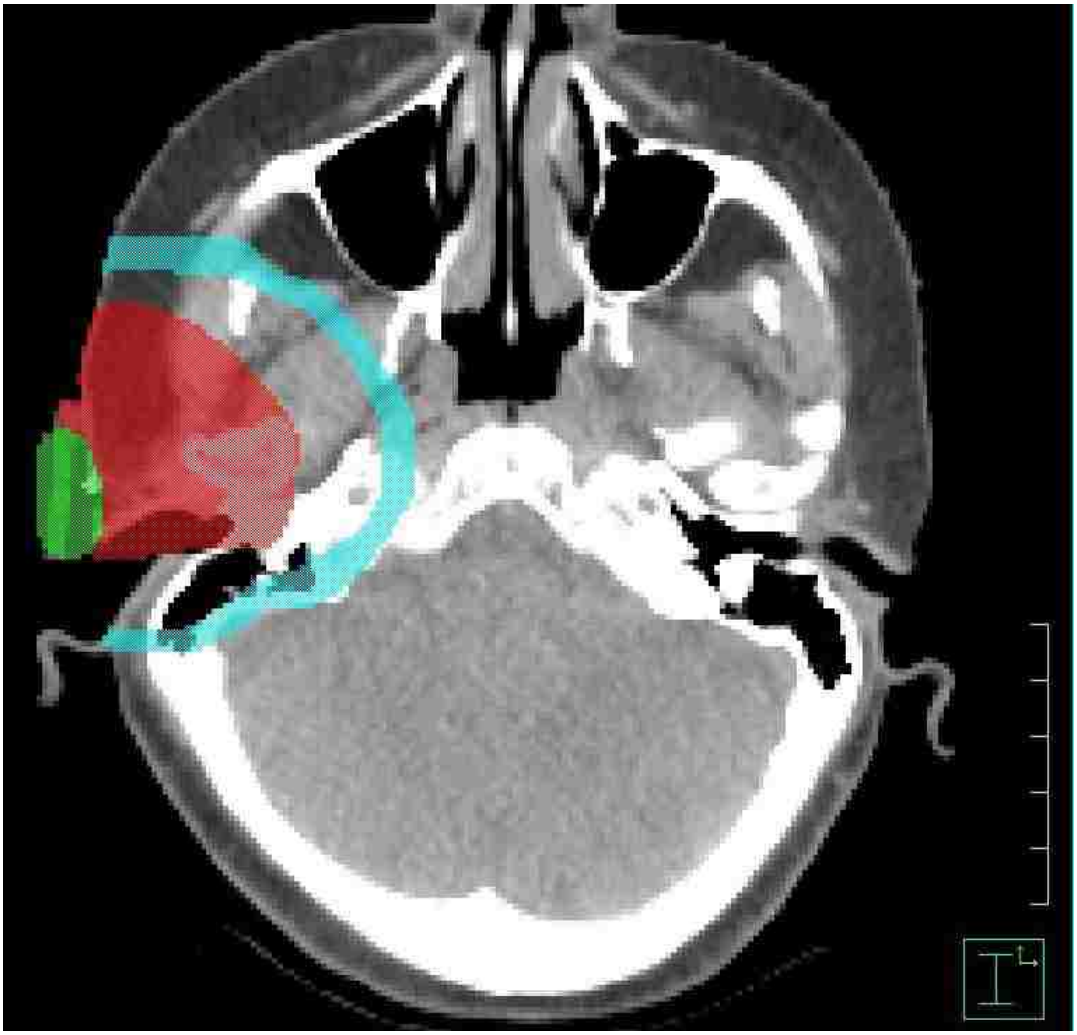

Figure 4. Example of dose limiting structures surrounding the PTV (red contour is the PTV, green contour is a hot spot, and blue contour is the ring)

Plan parameters were set to values most commonly used in the clinic to ensure that plan delivery would not exceed normal treatment and optimization times.

2.2.4.1 Helical tomotherapy

2.2.4.1.1 Jaw width:

In HT, the primary beam is collimated longitudinally by the jaws. The 'field width' parameter adjusts the longitudinal extent of the treatment field (full width at half maximum) at the machine isocenter. For all the TomoTherapy plans, the field width was set to the 2.45 cm jaw opening. This

setting was used to achieve good dose conformity to the PTV in the superior-inferior direction of the patient.

2.2.4.1.2 Pitch

Pitch is used to determine the amount of primary beam overlap along the longitudinal axis per gantry rotation. The pitch is related to the field width by the equation:

$$Pitch = \frac{Couch\ Distance\ Traveled\ per\ Gantry\ Rotation}{Field\ Width} \quad (1)$$

In order to minimize the HT thread effect (Kissick *et al.*, 2005), pitch values should be chosen such that

$$Pitch = 0.86 * \left(\frac{1}{n}\right), where\ n \in \{0,1,2,..\} \quad (2)$$

A larger pitch value decreases the amount of beam overlap and produces a slower gantry period. A smaller pitch value increases the amount of beam overlap and produces a faster gantry period. A pitch of 0.287 was ultimately chosen (n=3), in order to maintain DVH uniformity for tumor structures and keep the treatment times reasonable.

2.2.4.1.3 Modulation factor

The modulation factor is used by the optimizer to determine the range of intensity values of the primary beamlets. The modulation factor is calculated as the ratio of the greatest beamlet intensity for all

projections to the average intensity for all non-zero beamlets. The modulation factor effects the gantry period since beamlet intensity is affected by leaf open time. Essentially, this means a higher modulation factor increases the range of beamlet intensity (giving the optimizer more control over the dose distribution), however at the expense of a longer treatment duration. In this work, a maximum modulation factor of 3.0 was used which is a standard value used in the clinic.

2.2.4.1.4 Dose grid

The dose grid resolution was set to "normal" making the dimensions of the dose grid (3.91 x 3.91 x 2.5 mm^3). By selecting the normal dose grid, dose is calculated on the planning CT dataset that has been downsampled by a factor of 2. The CT data was imported into the TomoTherapy planning system at 256 x 256 pixel resolution; therefore, the dose grid resolution is (128 x 128).

Table 2. TomoTherapy plan parameter specifications.

Field width	2.45 cm
Pitch	0.287
Planning modulation factor	3
Dose grid resolution	normal (3.91 x 3.91 x 2.5 mm^3)

2.2.4.2 Mixed beam

2.2.4.2.1 Beam orientation

Pinnacle treatment plans were designed as a combination of a 5 or 7 field 6-MV IMRT (5 for the nasal cavity and 7 for the parotid gland) plan optimized on top of a single enface electron beam of energy 16 MeV (used on patient 2 to treat a shallow parotid tumor) or 20 MeV (all others). IMRT field configurations for a parotid patient can be seen in Figure 5. The enface electron beam was blocked and the PTV exposed with approximately a 1 cm margin. The exception to this was patient 3 (multiple PTVs); for that patient, the upper two PTVs were exposed and the lower PTV blocked to avoid treating

the lower neck. The lower PTV dose was primarily delivered by the supplementary IMRT fields. IMRT photon fields were roughly arranged around the body approximately every 30 degrees. When choosing beam angles, consideration was given to both entry and exit of beams in the patient.

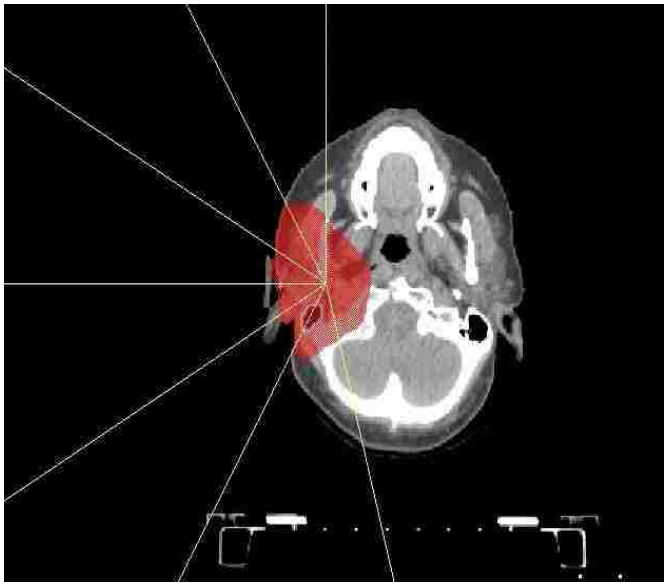

Figure 5 Transverse slice for patient 1with central beam axis orientation shown with straight lines. PTV is shown in red colorwash.

2.2.4.2.2 Beam ratios

Historically, mixed beam plans often involved a combination of photons and electrons with electrons, usually heavily in favor of electrons (Tapley, 1976). However it was unknown what ratio would be optimal when mixing electrons and IMRT. Therefore, seven different ratios of IMRT to electrons were investigated. The ratios examined are listed below and are calculated as a ratio of the dose to R_{100} of the electron beam. It should be noted that, for the purposes of this study, the IMRT-only and electron-only plans were considered subsets of the mixed beam planning approach.

- 1:0 (IMRT only)
- 2:1
- 1:1
- 1:2

- 1:3
- 1:4
- 0:1 (Electron only)

The dose grid resolution for the IMRT with electrons plans was set to 4.0 x 4.0 x 4.0 mm^3 on the Pinnacle treatment planning system. The extent of the dose grid was manually selected to cover OARs and PTVs plus a wide margin including 5 cm past this range.

Table 3. Plan parameter specifications.

Parameter	Parotid patients	Nasal cavity patients
Number of IMRT beams (energy)	7 (6MV)	5 (6 MV)
Number of electron beams (energy)	1 (20MeV or 16 MeV)	1 (20 MeV)
Lead skin collimation for electron beam	No	Yes
Water equivalent bolus used for HT	Yes (to boost surgical scar)	No

2.2.4.3 Optimization and Dose Calculation

The physician prescription for the planning target volumes were kept the same for the both the TomoTherapy plan and the mixed beam plan. The prescribed PTV dose ranged from 54 Gy to 70 Gy for the range of patients chosen for this study.

After defining the planning parameters, the treatment plans were optimized, and final doses calculated. Both planning systems use target and avoidance structure constraints in their optimization process. The planning goals for the HT plan and the mixed beam plan were kept as close as possible. Table 4 shows the optimization objectives for HT and the IMRT course of the mixed beam plans for the parotid tumor patients; Table 5 shows similar data for the nasal cavity tumor patients.

The optimization procedure for the mixed beam plans was as follows. For each trial, the ratio of the prescribed dose to R_{100} for the electron beam was chosen. The electron beam dose contributions were computed using an electron 3D algorithm with heterogeneous density correction. Following the dose computation for the electron beam, the dose constraints for the OARs and PTVs were set for the IMRT

photon fields. The intensity of the IMRT beams was modulated using a pencil beam optimization process set with a max number of iterations of 40. A collapsed cone convolution dose calculation, which is more accurate but slower than the pencil beam model, was computed at the 15th and final iterations. The majority of plans reached an optimal solution before the 40th iteration (Stopping tolerance was set as 1e-05).

Table 4 Dose objectives and planning prescriptions for parotid patients for targets and organs at risk for HT and mixed beam plans.

Variable	Patient 1	Patient 2	Patient 3
Targets:			
Prescription			
(Isocenter dose in Gy)	59.4	65.0	63.9
Planning goals			
PTV			(Primary; Secondary; Tertiary)
Minimum dose (Gy)/target volume (%)	59.4/98	65.0/98	63.9/98; 60.0/98; 54.0/98
Maximum dose	62.0	66.0	64.0; 61.0; 55.0
Minimum dose	59.0	64.0	62.5; 59.0; 53.0
Organs at risk:			
Maximum dose (Gy)/target volume (%)			
Spinal cord	42.0	41.0	41.0
$Parotid_{con}$	9.0/5	15.0	15.0
Eye_{isp}	3.0	12.0	5.0
Eye_{con}	3.0	12.0	5.0
$Lens_{ips}$		2.0	
$Lens_{con}$		2.0	
optic $nerve_{ips}$			50.0
$Auditory_{ips}$	60 & 50/30		
Brain stem	49.0		
Lips	15/10		12.0
Optic chiasm			50.0
Fifth cranial nerve			63.9 & 52.0/98
Spinal cord + margin			45.0

At the end of the optimization, the fluence maps generated were converted into MLC leaf sequences using a k-means clustering conversion with a maximum of 10 levels and a 3% error tolerance. The conversion constraints were that the minimum segment area set to 2 cm^2 and minimum segment

monitor units of 2, which are typical values found in the MBPCC clinical head and neck IMRT optimization protocol. The resulting plan was reviewed and the process was repeated after adjusting the weighting of each dose constraint as necessary. In general, the weighting of the OARs were set as high as possible without degrading the dose distributions to the PTV or surrounding normal tissue. Finally a segment weight optimization was done to ensure that optimal weighting of each segment after the conversion.

The optimization procedure for the HT plans was as follows. The TomoTherapy Hi-Art system optimization for PTVs was controlled using three dose constraint goals: 1) the percent volume of the primary PTV receiving a set dose. In this study that value was 98% of the PTV volume receiving the prescription dose. This is a hard constraint, in that the optimization will only return DVHs that meet this constraint. 2) The maximum dose delivered to the PTV and 3) minimum dose to the PTV (these values can be found in Table 4 and Table 5). OARs were controlled by the maximum dose to that OAR and the volume of the OAR to receive a certain dose. Similar to the mixed beam plans, the optimization process uses importance and penalties as a relative weight to update leaf intensity values during the iterations of the optimization.

HT plans were optimized using beamlet mode, which uses a pre-computed dose distribution for each beamlet and convolves the dose spread kernel with an interaction point. After roughly 40 iterations, the optimization was paused. Penalties and the importance of the PTV and OARs were evaluated and adjusted as needed. The optimization was then restarted and allowed to continue for another 20 to 40 iterations. This process was repeated until acceptable results were achieved in the DVH.

When the PTV reached the point where it would no longer improve in conformity and was within the desired objectives, the OARs were increased in weighting until they adversely affected the PTV's dose objectives. When the PTV was within the desired objectives and OARs reduced to clinically acceptable values, the HT optimization process was terminated. Table 6 lists typical PTV, OAR, and ROI objectives upon completion of optimization. Finally, a final full scatter calculation was performed.

Table 5. Dose objectives and planning prescriptions for nasal cavity patients for targets and organs at risk for HT and mixed beam plans.

Variable	Patient 1	Patient 2
Targets:		
Prescription		
(isocenter does in Gy)	70.0	65.0
Planning goals		
Primary PTV		
Minimum dose (Gy)/target volume (%)	70.0/98	65.0/98
Maximum dose	71.0	65.8
Minimum dose	69.0	64.0
Organs at risk:		
Maximum dose (Gy)/target volume (%)		
Spinal cord	41.0	41.0
Right eye	35.0	20.0
Left eye	35.0	20.0
Right lens/Anterior of eye	12.0	5.0
Left lens/Anterior of eye	12.0	5.0
Right optic nerve	45.0	
Left optic nerve	45.0	

Table 6 Typical PTV, OAR, and ROI constraints upon completion of optimization

Structure	Importance	Max Dose (Gy)	Max Dose Penalty	DVH Vol (%)	DVH Dose (Gy)	DVH Penalty	Min Dose (Gy)	Min Dose Penalty
PTV	50	62	4	98	59.4	1	59.0	1
Contralateral Parotid	1	12	6	5	5	2	-	-
Spinal Cord	5	42	25	10	10	1	-	-
Eyes	2	3	1	10	2	1	-	-
Brainstem	2	49	3	40	30	1	-	-
Ring	1	35	1	10	34	1	-	-

After the final dose full scatter calculation, the dose matrix from the Hi-Art system was imported into the Pinnacle patient database such that the isodose plots and DVHs from the HT plan could be displayed and compared with mixed beam plans.

2.3 Aim 3: Evaluation of Endpoints - Evaluate and Compare each Plan Based on *Clinical*, *Dosimetric*, and *Biological* Endpoints.

2.3.1 Clinical Evaluation

In order to evaluate the plans on their clinical effectiveness, a radiation oncologist compared and rated each plan. The radiation oncologist reviewed each patient's isodose distribution and DVHs, and was then asked to fill out a worksheet/questionnaire related to the quality of the plans (located in the Appendix A).

In the questionnaire, the radiation oncologist was first asked to rate the clinical utility of each plan using the following choices: acceptable, marginally acceptable, indifferent, marginally unacceptable, and unacceptable. Second, the radiation oncologist was asked to assess the TomoTherapy plan relative to the best IMRT with electron plan (this included IMRT-only and electron-only plans} using the following choices: superior, marginally superior, indifferent, marginally inferior, and inferior. Next, the radiation oncologist was asked to list the reasons why he/she found the plan he chose superior. Finally, a margin was left on the questionnaire for additional comments.

2.3.2 Dosimetric Evaluation

In order to evaluate the dose distribution in the plans, several dosimetric endpoints were computed. The dosimetric endpoints of interest in this study include:

- DVHs for each PTV and OAR
- Target volume coverage
- Conformity index (CI)
- Dose homogeneity index (DHI), the difference in PTV dose that 1% of the volume and 99% of the volume receives
- Maximum dose, mean dose, and relevant volume of OAR receiving a set dose based on complications

DVHs provide a summary of the entire dose distribution for a target volume and OARs. It effectively displays the percent of volume of the structure that may have been over and/or under-dosed. The DVHs, in conjunction with the spatial information contained in an isodose dose distribution, provide tools needed to compare competing plans.

Target volume coverage was computed for all planning target volumes. Maximum dose was defined as the highest dose to 1% of the target volume, $D_{max(v1\%)}$. Minimum dose was defined as the lowest dose to 99% of the target volume, $D_{min(v99\%)}$ or greater. This was done to avoid artificially small hot or cold spots that might result from dose algorithm approximations or dose grid placements, as these inhomogeneities spots might not be considered clinically meaningful.

The conformity index (CI) is a tool for scoring and evaluating different treatment plans for the same patient. CI has been defined in different ways (Feuvret *et al.*, 2004). However, CI for this study was computed using the method of Paddick (Paddick, 2000), to take into account the dose coverage of the PTV. The method combines the proportion of the target volume covered by the prescription isodose with the proportion of the prescription isodose within the target volume, as described following equation:

$$CI = \frac{{TV_{PIV}}^2}{TV \times PIV}, \quad (3)$$

where TV is the volume of the target, TV_{PIV} is the volume of the target within the prescribed isodose value, and PIV is the volume covered by the prescribed isodose value. In an ideal treatment plan, the CI would equal to 1, with values less than 1 reflecting less conformal plans.

In order to quantify the dose uniformity in the PTV, difference between the maximum dose (that is the dose that only 1% of the PTV receives) and the minimum dose (that is the dose that 99% of the PTV receives) was computed. The difference in dose was then divided by the desired target dose, and this value is known as the dose homogeneity index (DHI). DHI was defined as $(D_{max(v1\%)} - D_{min(v99\%)})/ D_p$ where $D_{max(v1\%)}$ and $D_{min(v99\%)}$ represent the doses to 1% and 99% of the PTV, respectively. For example,

$D_{99\%}$ indicates that at least 99% of the target volume receives dose, D, and hence $D_{max(v1\%)}$ and $D_{min(v99\%)}$ are considered to be maximum and minimum doses, respectively. D_p is the desired target dose. Smaller values of the DHI represent more uniform dose distributions and are thus better. This metric will be used to test the hypothesis.

2.3.3 Biological Evaluation

Dosimetric evaluations effectively convey the amount of dose deposited, however a biological evaluation can give information related to how the dose might affect the patient. Radiobiological metrics such as normal tissue complication probability (NTCP) and tumor control probability (TCP) were used to compare plans. An in-house radiobiological program developed by Tae Ku Lee, Ph.D., research medical physicist at our clinic, was used to compute NTCP and TCP values. NTCP values were computed using the Lyman-Kutcher-Burman probit model (Lyman, 1985) (Kutcher and Burman, 1989) such that

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} e^{-\frac{1}{2}*x^2}\, dx \tag{4}$$

and

$$t = \frac{D - TD_{50}(v)}{m * TD_{50}(v)}, \tag{5}$$

where D is the dose that uniformly irradiates the volume, $TD_{50}(v)$ is the dose that produces a 50% complication rate for uniform irradiation of the fractional volume, m is a modeling parameter that sets the steepness of the dose response curve. v is the ratio of organ uniformly irradiated and is defined as

$$v = \frac{V}{V_{OAR}}, \tag{6}$$

V is the volume of the OAR uniformly irradiated and V_{oar} is the volume of the OAR.

$$TD_{50}(v) = \frac{TD_{50}(1)}{v^n}, \tag{7}$$

where n is a parameter to account for volume effects for an organ. Small values of n indicate a smaller effect from the volume irradiated such as in a serial structure like the spinal cord, which can be damaged with high doses in small volumes. Values of n, m, and TD_{50} for OARs in this work were taken from available literature (Emami *et al.*, 1991; Burman *et al.*, 1991; Roesink *et al.*, 2001) and are shown in Table 7.

Table 7. Values of the biologic parameters used for calculation of normal tissue complications probabilities(Burman *et al.*, 1991; Roesink *et al.*, 2001; Eisbruch *et al.*, 1999)

Organ (endpoint)	n	M	TD50 (whole organ)
Spinal cord (myelitis/necrosis)	0.05	0.175	66.5
Optic nerve (blindness)	0.25	0.14	65
Eye/retina (blindness)	0.2	0.19	65
Lens (cataract)	0.3	0.27	18
Parotid (xerostomia)	0.7	0.18	46
Parotid (salivary flow reduction to <25% at 6 wk)	1	0.54	31
Parotid (salivary flow reduction to <25% at 1 year)	1	0.45	39

TCP values were computed for the primary PTV using the standard Poisson dose-response model (Steel, 2002) assuming homogeneous tumor cell distribution:

$$TCP = exp\left[-\rho * TV * \left(e^{-\alpha D-\beta dD} + \ln 2\frac{(T_{tot} - T_k)}{T_p}\right)\right], \quad (8)$$

where ρ is the average density of tumor cells in the target, TV is the tumor volume, α is the cell radiosensitivity, β is the effectiveness/lethality of radiation, D is the total treatment dose, d is the dose per fraction, T_{tot} is the overall time of treatment, T_k is the "kick-off" time for the cell proliferation, and T_p is the average doubling time of clonogenic cells in the tumor. Parameters used in the TCP calculation are shown in Table 8 and were taken from available literature (Fowler, 2001; Wigg, 2001; Lee *et al.*, 2008).

Table 8. Parameters selected to calculate TCP for head and neck patients (Wigg, 2001; Fowler, 2001)

ρ	average density of tumor cells in the target	1.5 x 10^4 cm^{-3}
α	cell radio sensitivity	0.35 (Gy^{-1})
B	the effectiveness/lethality of radiation	0.035 (Gy^{-2})
T_k	time for cell proliferation	28
T_p	average doubling time of clonogenic cells	3

2.3.4 Secondary Cancers

In order to estimate the secondary cancer probabilities, measurements of the volume of normal tissue receiving lower doses were made. The volume of tissue receiving between 5 and 25 Gy is thought to be significant because of the high estimated solid cancer incidence within that dose interval (Schneider and Kaser-Hotz, 2005). Figure 6 shows a plot of cancer incidence per 10^4 per year for solid tumor induction as a function of dose. From this figure, note that at higher doses there is a lower chance of secondary cancer induction due to mutated cells

becoming sterilized. The volume of tissue receiving between 25 Gy and 5 Gy provides a general estimation of secondary cancer induction.

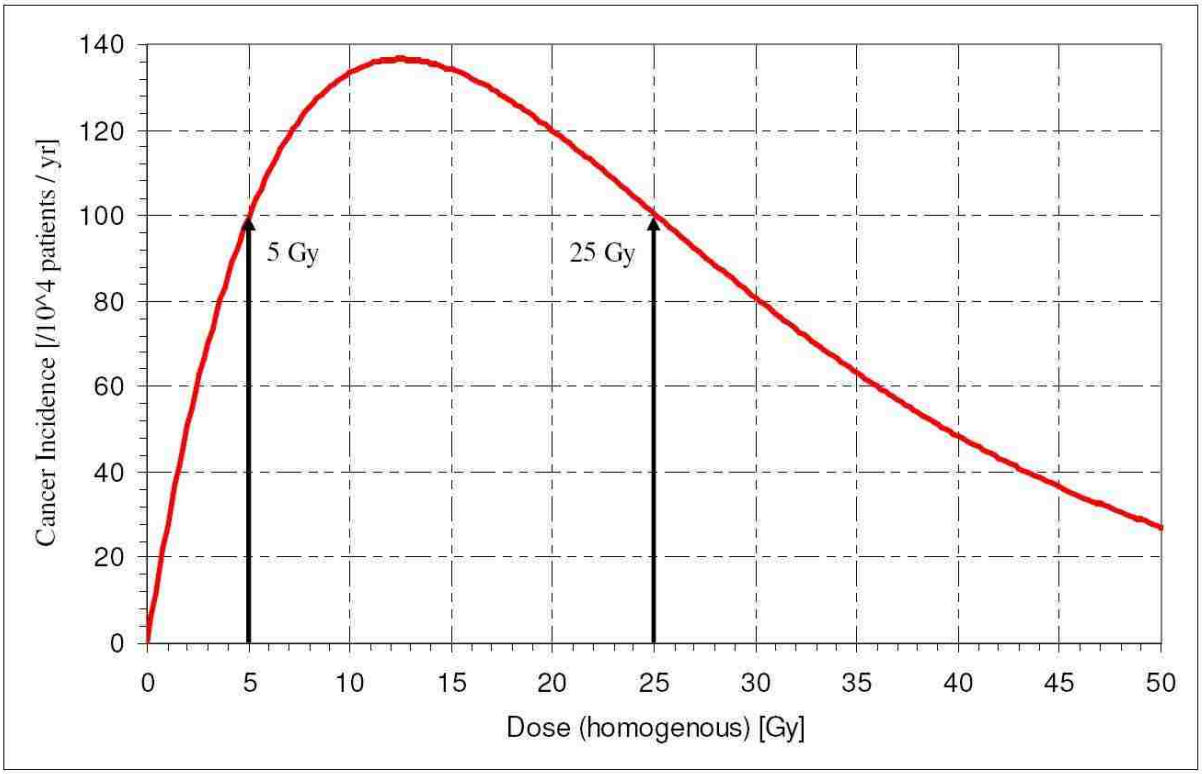

Figure 6 Estimated solid tumor induction as a function of homogenous organ dose for normal tissue based on the Schneider's model (Schneider and Kaser-Hotz, 2005)

Chapter 3 Results

3.1 Convention for Presenting Results of Each Patient

The format for presenting the results is the same for all patients. For each patient, the results are presented in the following order:

- Review of patient diagnosis and critical patient information
- Isodose distribution comparison
- DVH comparison
- Radiation oncologist's review
- Dose statistics of the PTV and the resultant TCP
- Dose statistics of the OARs and the resultant NTCPs and secondary cancer induction

Isodose distributions are shown in orthogonal planes at the geometric center of the primary PTV. The isodose distributions are displayed for the TomoTherapy, IMRT, and the mixed beam ratio judged to exhibit the best balance of PTV coverage and OAR sparing. A full set of isodose distributions for all mixed beam plans are shown in Appendix B. The isodose lines are displayed in units of cGy and correspond to the following values:

- 115% of the PTV prescription (maroon)
- 105% of the PTV prescription (yellow)
- 100% of the PTV prescription (red)
- 95% of the PTV prescription (purple)
- 45 Gy, a critical dose for the myelitis and necrosis of the spinal cord (green)
- 35 Gy, a critical dose for blindness for the eyes (steel blue)
- 25 Gy, doses between 5 and 25 Gy have a high probability of solid tumor induction, (grayscale)
- 5 Gy, see above, (olive)

The DVH comparison for each patient begins with a description of all mixed beam plans. This is followed by a comparison of DVHs for the HT, IMRT, and select mixed beam plans.

3.2 Patient One - Parotid

3.2.1 Patient Specific Information

A 53 year old female was diagnosed to have intermediate grade mucoepidermoid carcinoma in the right parotid gland, stage T1N0M0. Patient had close margins following surgery and has primarily a risk of recurrence within the parotid bed. She was at low risk of developing distant metastases. 59.4 Gy at 2 Gy per fraction was delivered using IMRT.

3.2.2 Isodose Distributions

Isodose distributions for HT, IMRT (1:0), and a selected mixed beam plan (1:2 ratio) are displayed in Figures 7-9. The white crosshairs in the CT images indicate the position of the orthogonal planes and the red colorwash region indicates the primary PTV. The red isodose line represents the desired prescription dose (59.4 Gy) to the primary PTV. Dose statistics for the isodose distributions can be found in Table 9 for the PTV and Table 11 for the critical structures.

3.2.2.1 HT

The HT isodose distribution showed more conformal coverage of the PTV than the IMRT and mixed beam plans. Hot spots in the HT plan were small (~5%) and were generally located along the skin surface. These 5% hotspots (62.4 Gy), are observable as the yellow isodose lines. In Figure 7, can be seen both the transverse and coronal slices.

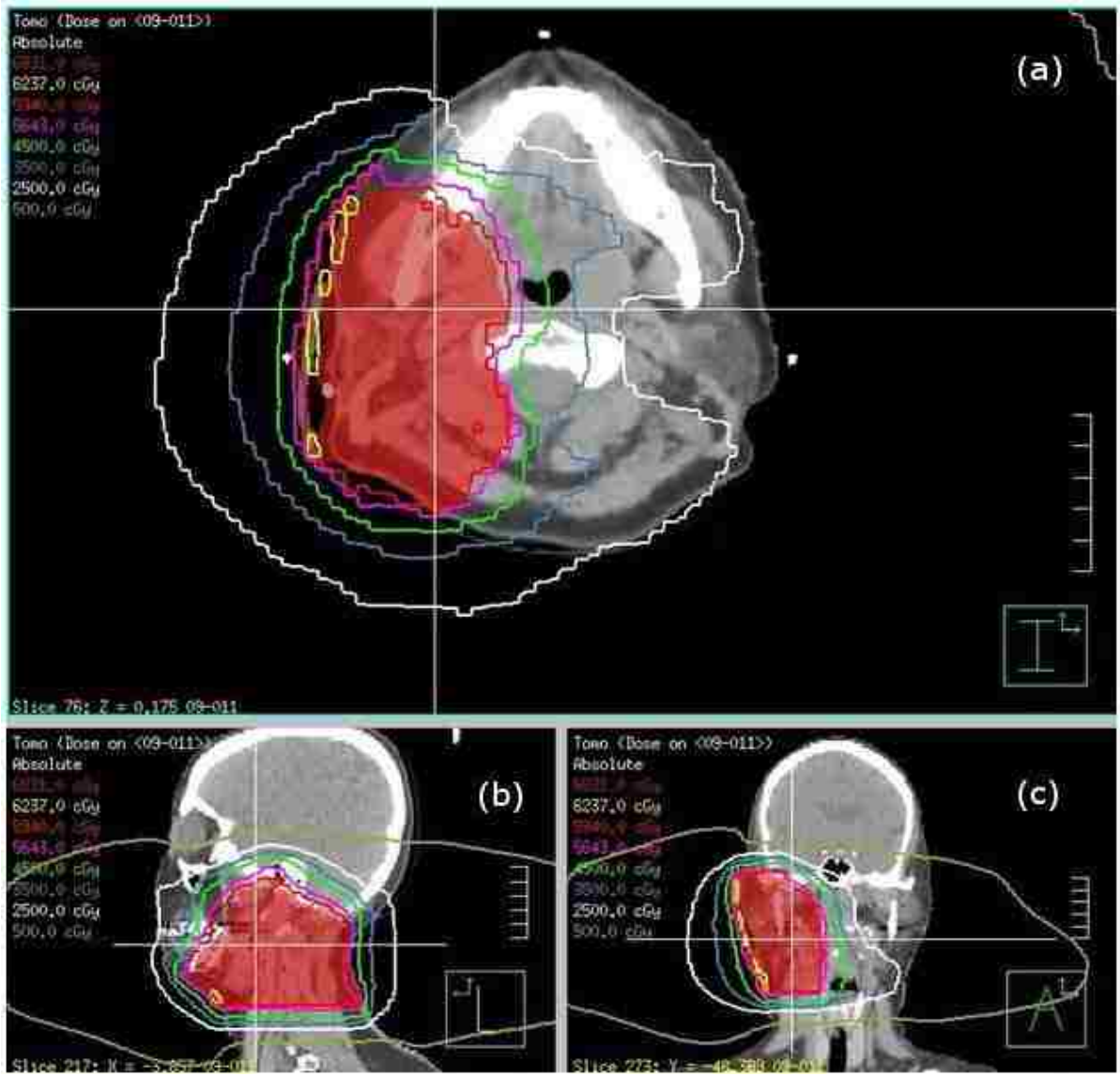

Figure 7 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 1 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

No cold spots were noted in the PTV in the HT plan. The HT plan showed a good dose fall off towards the contralateral side of the head where the plan was optimized to avoid the contralateral parotid gland. The 25 Gy isodose line can be seen wrapping around the contralateral parotid in the HT plan as a result of the optimization. Near the PTV, the dose fall off for the HT plan was similar to both the IMRT and the mixed beam plan.

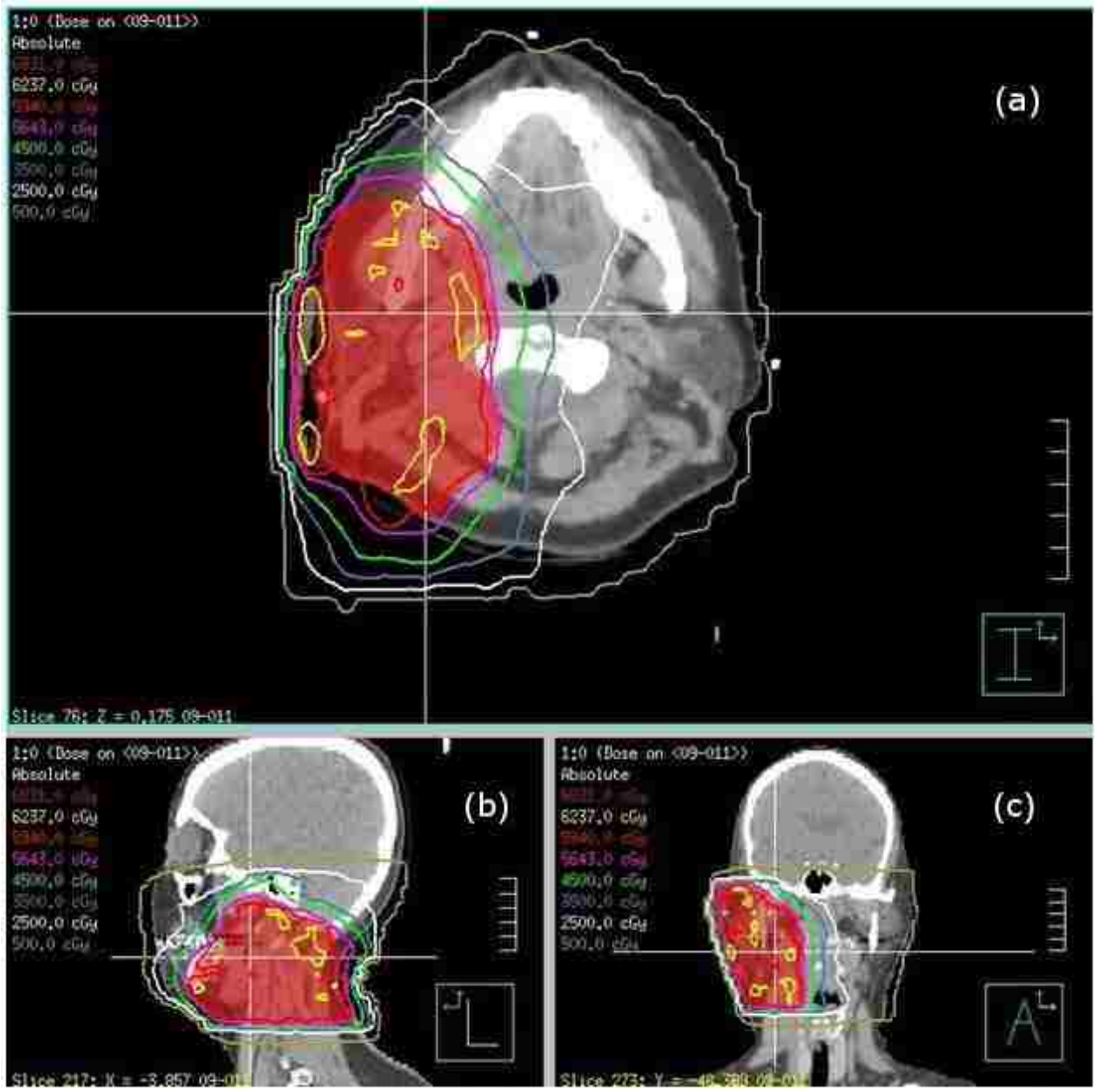

Figure 8 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 1 for the IMRT (1:0) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The HT plan showed a significantly larger area of tissue outside the PTV receiving a dose lower than 35 Gy compared to the mixed beam plan. However the volume of normal tissues receiving between 25 Gy and 5 Gy in the HT plan was less than in the IMRT and mixed beam plan.

3.2.2.2 IMRT/Mixed Beam

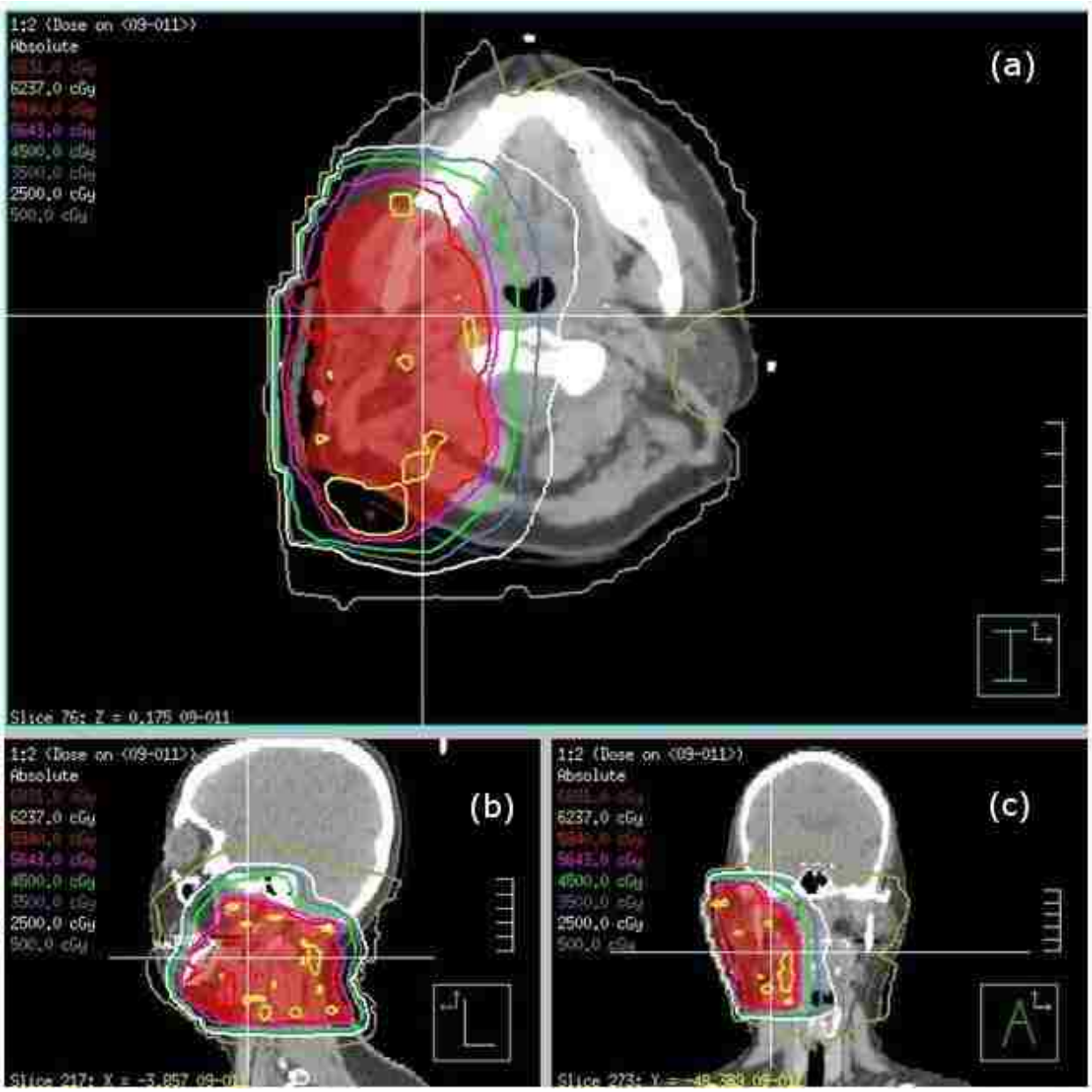

Figure 9 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 1 for the IMRT + electron (1:2) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The IMRT (Figure 8) and selected mixed beam (Figure 9) isodose distributions showed distinct hot and cold spots. The IMRT plan, similar to the HT plan, shows two 5% hot spots near the surface on the transverse slice but also shows small hot spots intermittently throughout the PTV and hot spots at the anterior and posterior edge of the foramen magnum. For the mixed beam plan, a 5% hot spot is visible

on the posterior curvature of the neck. The dose to the medial edge of the PTV near the spinal cord in the IMRT and mixed beam plan falls below the prescription dose (~5% cold spot), likely a outcome of constraining dose to the spinal cord, which abuts the PTV. In addition, the prescription isodose line for the mixed beam plan doesn't cover the entire PTV at the anterior edge, resulting in a slight (95% coverage) cold spot.

The IMRT and mixed beam plan isodose distributions exhibited similar fall off near the PTV compared the HT plan, but a sharper dose fall off away from the PTV. The three plans show similar dose fall off near the PTV with the mixed beam plan showing a slightly faster fall off to 35 Gy (steelblue line) than IMRT or HT.

3.2.3 DVH Comparisons

3.2.3.1 All mixed beam plans

DVH comparisons for the PTV and OARs for the mixed beam plans are shown in Figure 10 and Figure 11, respectively. The mixed beam plans all showed similar PTV dose volume coverage with the exception of the 0:1 ratio (electron only) plan, which was significantly less uniform. Of the mixed beam plans, the 2:1 ratio (black line) had the steepest curve (an indication of conformity), while the 1:1 ratio (red line) had the worst, excluding the electron only.

For the OARs, the 0:1 ratio plan gave the lowest mean and max dose to the brainstem and the contralateral parotid, followed by the 1:4 ratio mixed beam plan. All mixed beam plans showed similar dose-volume relationships for the brainstem over 50 Gy. For the contralateral parotid gland, the 2:1 and 1:1 mixed beam similarly gave a mean dose that was larger than the other mixed beam plans. The 1:2 ratio plan showed good balance of PTV coverage and critical structure sparing.

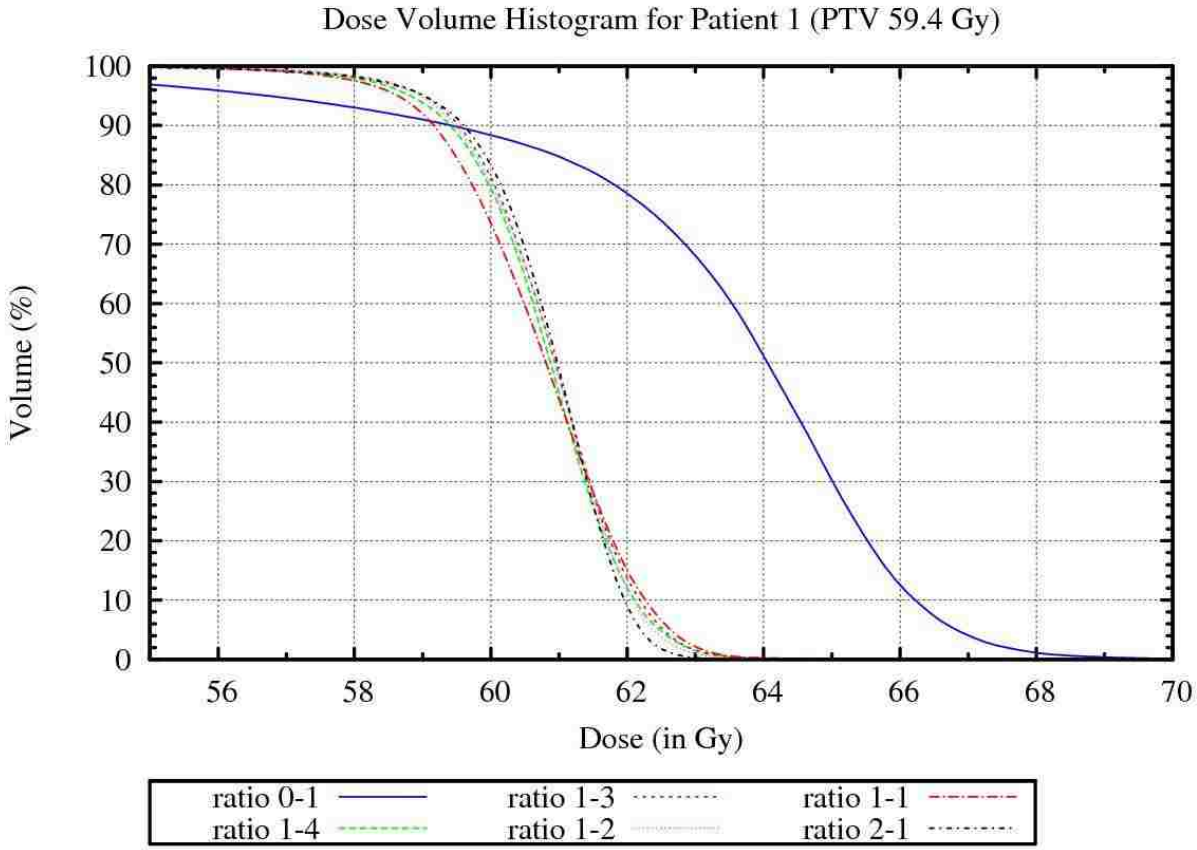

Figure 10 DVHs for patient 1 for the PTV of the mixed beam plans

3.2.3.2 Select mixed beam, HT, and IMRT

DVHs for the PTV and OARs for the HT, IMRT, and selected mixed beam (1:2 ratio) are shown in Figure 12. The HT plan showed a smaller volume of PTV receiving greater than and less than the prescription dose of 59.4 Gy compared to the IMRT and mixed beam plans (this is reflected in the isodose of Figure 7). The HT plan showed a more uniform dose distribution in the PTV.

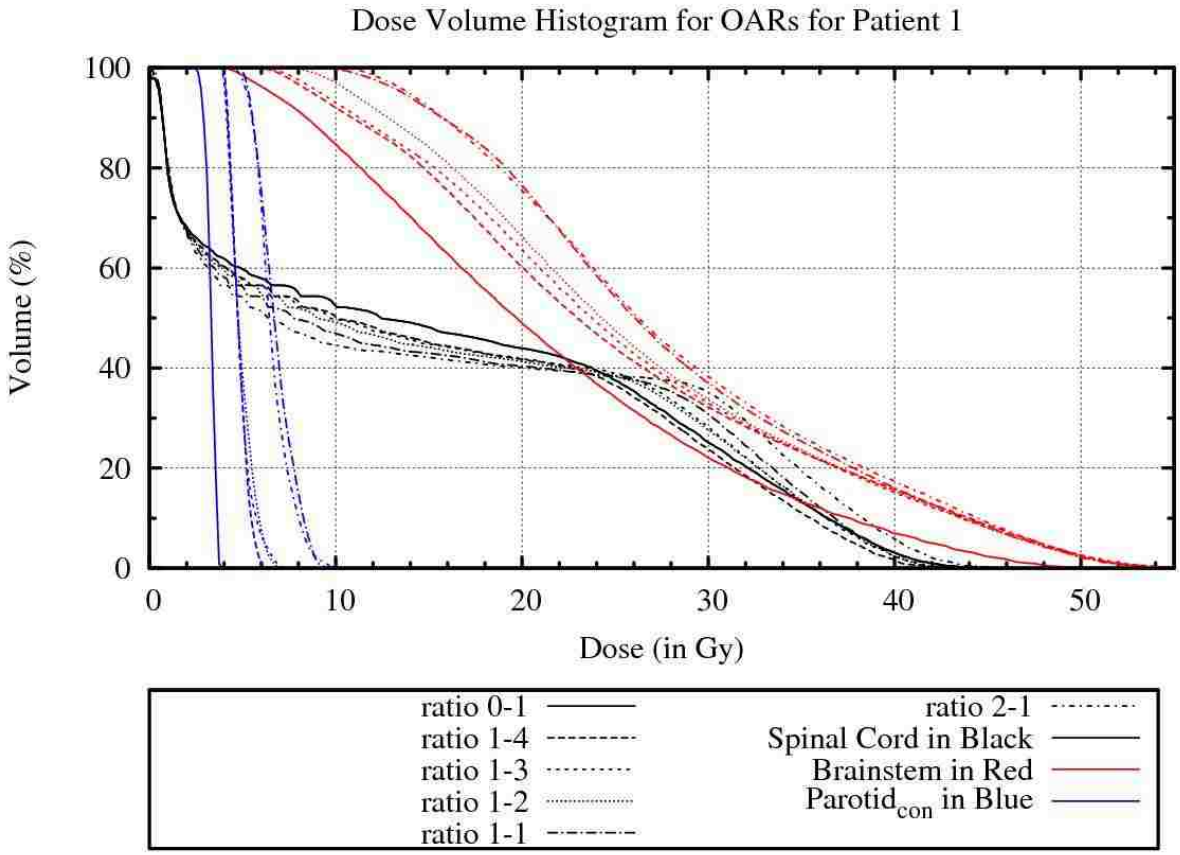

Figure 11 DVHs for patient 1 for the OARs of the mixed beam plans

For the OARs, the HT and mixed beam plans had a similar maximum spinal cord, which was lower than maximum dose from the IMRT plan. The volume of brainstem receiving above 50 Gy was lowest for the HT plan. However, the mixed beam plan gave the lowest integral dose for the brainstem. The brainstem DVHs cross at about 40 Gy. The selected mixed beam plan showed less volume of brainstem receiving over 50 Gy than the IMRT plan. Overall, the HT plan showed good sparing of the spinal cord and the brainstem (above 40 Gy).

3.2.4 Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of the HT, IMRT, and mixed beam plans and found the HT plan to be clinically acceptable, was indifferent about the IMRT plan, and found the best mixed beam ratio to be marginally acceptable.

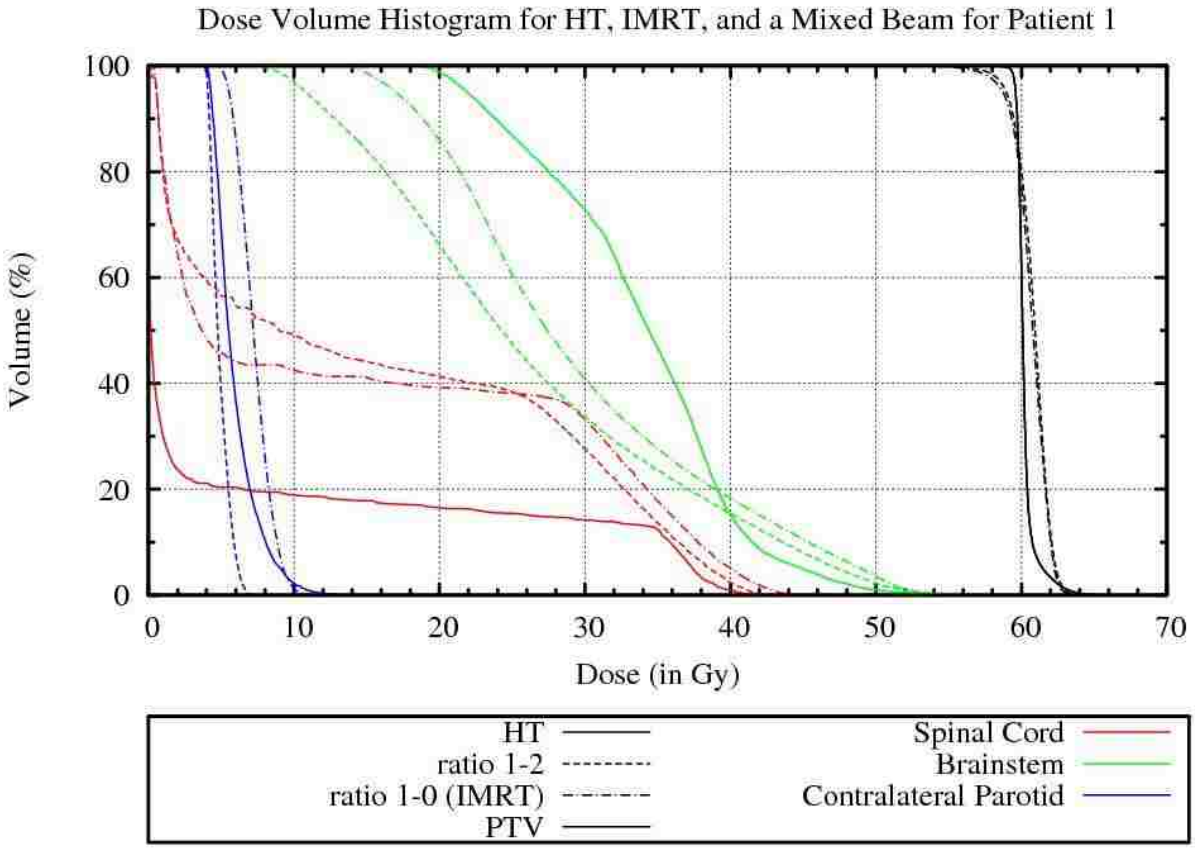

Figure 12 DVHs for patient 1 for the PTV and OARs for the HT, IMRT, and selected mixed beam plans

A complete list of individual plan reviews can be found in Appendix A. After reviewing the dose distributions and DVHs for all the plans, he ranked the TomoTherapy plan marginally superior to the mixed beam plan. PTV coverage was listed as a reason for preferring HT plan over the mixed beam. The radiation oncologist suggested that a larger volume of brainstem receiving a high dose may be of concern.

3.2.5 Dose Statistics for the PTV and TCP

3.2.5.1 All mixed beam plans

Table 9 gives the dose statistics for the PTV for the mixed beam plans. The TCP values were comparable (within ± 0.1% of 98.6% tumor control) for all the plans, except for the electron-only plan (95.6%). Conformity index (CI) was highest for the 2:1 ratio plan (0.852) followed closely by the IMRT plan with 0.842. CI generally decreased as more electrons were introduced and was lowest (worst) for the electron-only plan (0.656). However, the addition of a small IMRT component to the electron plan significantly improved CI (0.814 for the 1:4 ratio). Dose homogeneity index was similar for all mixed beam plans, with a high value of 0.102 (worst) and a low value of 0089 (best) for the 1:1 and 1:2 ratios, respectively.

Table 9 Dose statistics for the PTV for the mixed beam plans for patient 1

PTV – Patient 1					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
1:0 (IMRT)	98.6	0.842	0.097	62.7	56.9
2:1	98.7	0.852	0.09	62.3	57.3
1:1	98.6	0.798	0.102	63.2	57.1
1:2	98.7	0.832	0.089	62.9	57.6
1:3	98.7	0.818	0.094	63	57.5
1:4	98.7	0.814	0.099	63.1	57.3
0:1	95.6	0.656	0.271	68.1	52.0

3.2.5.2 Select mixed beam, HT, and IMRT plans

Table 10 gives the dose statistics for the PTV from the HT, IMRT, and select mixed beam plans. The TCP values were within ± 0.1% of 98.6% tumor control. The CI for the IMRT plan was slightly lower than the HT and mixed beam plans (0.842 compared to 0.851 and 0.832, respectively). The HT plan showed a lower DHI value, indicating the HT plan was more homogeneous over the PTV.

Table 10 Dose statistics for the PTV for the HT, IMRT, and select mixed beam plan for patient 1

PTV – Patient 1					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
HT	98.5	0.851	0.063	63.2	59.4
1:0	98.6	0.842	0.097	62.7	56.9
1:2	98.7	0.832	0.089	62.9	57.6

3.2.6 Dose Statistics for OARs and NTCP

Table 11 Dose statistics for the OARs for the mixed beam plans for patient 1

Critical Structures – Patient 1									
	Contralateral parotid		Spinal cord		Brainstem		Lips	Contralateral eye	Ipsilateral eye
Plan	Dmean	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	Dmax	Dmax
1:0	7.3	7.9	45.3	0.5	55.8	0.1	24.4	2.9	4.4
2:1	6.7	7.3	46.6	0.6	55.6	0.1	18.3	3.2	4.0
1:1	6.9	7.5	48.1	0.5	56.1	0.1	14.6	3.6	4.1
1:2	5.0	6.0	43.8	0.4	56.5	0.1	14.7	3.5	3.7
1:3	4.9	6.0	44.2	0.4	56.4	0.1	14	3.5	3.7
1:4	4.9	5.9	43.9	0.3	56.4	0.1	17.3	3.6	3.8
0:1	3.4	4.9	45.0	0.4	51.8	<0.1	13.3	3.6	3.9

Table 12 Dose statistics for the OARs for the HT, IMRT, and select mixed beam plan for patient 1

Critical Structures – Patient 1									
	Contralateral parotid		Spinal cord		Brainstem		Lips	Contralateral eye	Ipsilateral eye
Plan	Dmean	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	Dmax	Dmax
HT	6.0	6.8	43.2	0.3	59.6	0.1	23.1	6.9	9.1
1:0	7.3	7.9	45.3	0.5	55.8	0.1	24.4	2.9	4.4
1:2	5.0	6.0	43.8	0.4	56.5	0.1	14.7	3.5	3.7

3.2.6.1 Contralateral parotid

3.2.6.1.1 All mixed beam plans

Table 11 gives the dose statistics for the contralateral parotid for the mixed beam plans. Mean dose and NTCP of salivary flow reduction to less than 25% at six weeks was computed. Mean dose values ranged from 7.3 Gy for the 1:0 (IMRT only) to 3.4 Gy for the 0:1 (electron only). For all but the 1:1 plan, there is a gradual reduction in the mean dose and the NTCP as electrons were introduced into the mixed beam ratio. However, adding electron beyond the 1:2 ratio only provided slight differences in the mean dose and the NTCP.

3.2.6.1.2 Select mixed beam (1:2), HT, and IMRT plan

Table 12 gives the dose statistics for the contralateral parotid for the HT, IMRT, and select mixed beam plan. Mean dose and NTCP of salivary flow reduction to less than 25% at six weeks was computed. Mean dose values were 6.0 Gy for HT, 7.3 Gy for IMRT, and 5.0 Gy for the select mixed beam plan. The mixed beam plan delivered 1 Gy less to the contralateral parotid than the HT plan, corresponding to a reduction in NTCP of about 1% in the contralateral parotid.

3.2.6.2 Brainstem

3.2.6.2.1 All mixed beam plans

Table 11 gives the dose statistics for the brainstem for the mixed beam plans. Maximum dose and NTCP of necrosis was computed. Maximum dose values ranged from 56.5 Gy for the 1:2 ratio to 51.8 Gy for the 0:1 (electron only) plan. NTCP for necrosis was similar for plans at 0.1%. Adding increased electron ratios did not reduce the NTCP for the brainstem (except for the electron only plan).

3.2.6.2.2 Select mixed beam, HT, and IMRT plan

Table 12 gives the dose statistics for the brainstem for the HT, IMRT, and select mixed beam plan. Maximum dose and NTCP of necrosis was computed. Maximum dose values were 59.6 Gy for HT, 55.8 Gy for IMRT, and 56.5 Gy for the select mixed beam plan. The NTCP values for the HT and IMRT plan were similar (0.1%), and were near that of the mixed beam plan (0.1%).

3.2.6.3 Spinal Cord

3.2.6.3.1 All mixed beam plans

Maximum dose and NTCP of necrosis/myelitis was computed. Maximum dose values ranged from 48.1 Gy for the 1:1 ratio to 43.8 Gy for the 1:2 ratio. NTCP for necrosis/myelitis was highest for the 2:1 plan at 0.6% and lowest for the 1:4 ratio plan (0.3%). There did not appear to be a strong coloration between increased electron involvement and decreased risk of a spinal cord complication.

3.2.6.3.2 Select mixed beam, HT, and IMRT plan

Table 12 gives the dose statistics for the spinal cord for the HT, IMRT, and select mixed beam plan. Maximum dose and NTCP of necrosis/myelitis was computed. Maximum dose values to the spinal cord were 43.2 Gy for HT, 45.3 Gy for IMRT, and 43.8 Gy for the select mixed beam plan. The NTCP values for the HT and select mixed beam plan were similar (0.3% and 0.4% respectively) and the IMRT plan's NTCP was slightly higher than HT and mixed beam at (0.5%).

3.2.6.4 Eyes and Lips

3.2.6.4.1 All mixed beam plans

Table 11 gives the dose statistics for the lips and eyes for the mixed beam plans. Maximum dose was computed for these OARs. The maximum dose to the lips was lower with the mixed beam and

electron only plans than the IMRT only plan. As expected, the dose to the ipsilateral eye was slightly higher than the contralateral eye. The IMRT only plan gave the lowest contralateral eye dose (2.9 Gy) but also gave the highest ipsilateral eye dose (4.4 Gy).

3.2.6.4.2 Select mixed beam, HT, and IMRT plan

Table 12 gives the dose statistics for the lips and eyes for the HT, IMRT, and select mixed beam plan. Maximum dose was computed. Maximum dose values for the lips were similar for the HT and IMRT plans (23.1 Gy and 24.4 Gy respectively), and were higher than the select mixed beam plan (14.7 Gy). Maximum dose to the eyes was higher with HT than either IMRT or the select mixed beam plan.

3.2.7 Non-specific Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 1129 cm^3 for the HT plan, 1232 cm^3 for the IMRT plan, and 1183 cm^3 for the mixed beam plan. The difference in volume between the HT and the mixed beam plan was 54 cm^3. Normalizing the volumes to the HT plan, the mixed beam plan gave 105% volume.

3.3 Patient Two - Parotid

3.3.1 Patient Specific Information

A 80 year old male was diagnosed to have squamous cell carcinoma in the left preauricular area, unstaged. He received postoperative radiotherapy delieverd primarily with 12 MeV to 65 Gy in 32 fractions.

3.3.2 Isodose Distributions

Isodose distributions for HT, IMRT (1:0), and the selected mixed beam plans (1:1 ratio and 1:4 ratio) are displayed in Figure 13-16. The white crosshairs in the CT images indicate the position of the

orthogonal planes and the red colorwash region indicates the primary PTV. The red isodose line represents the desired prescription dose (65.0 Gy) to the primary PTV. Dose statistics for the isodose distributions can be found in Table 14 for the PTV and Table 16 for the critical structures.

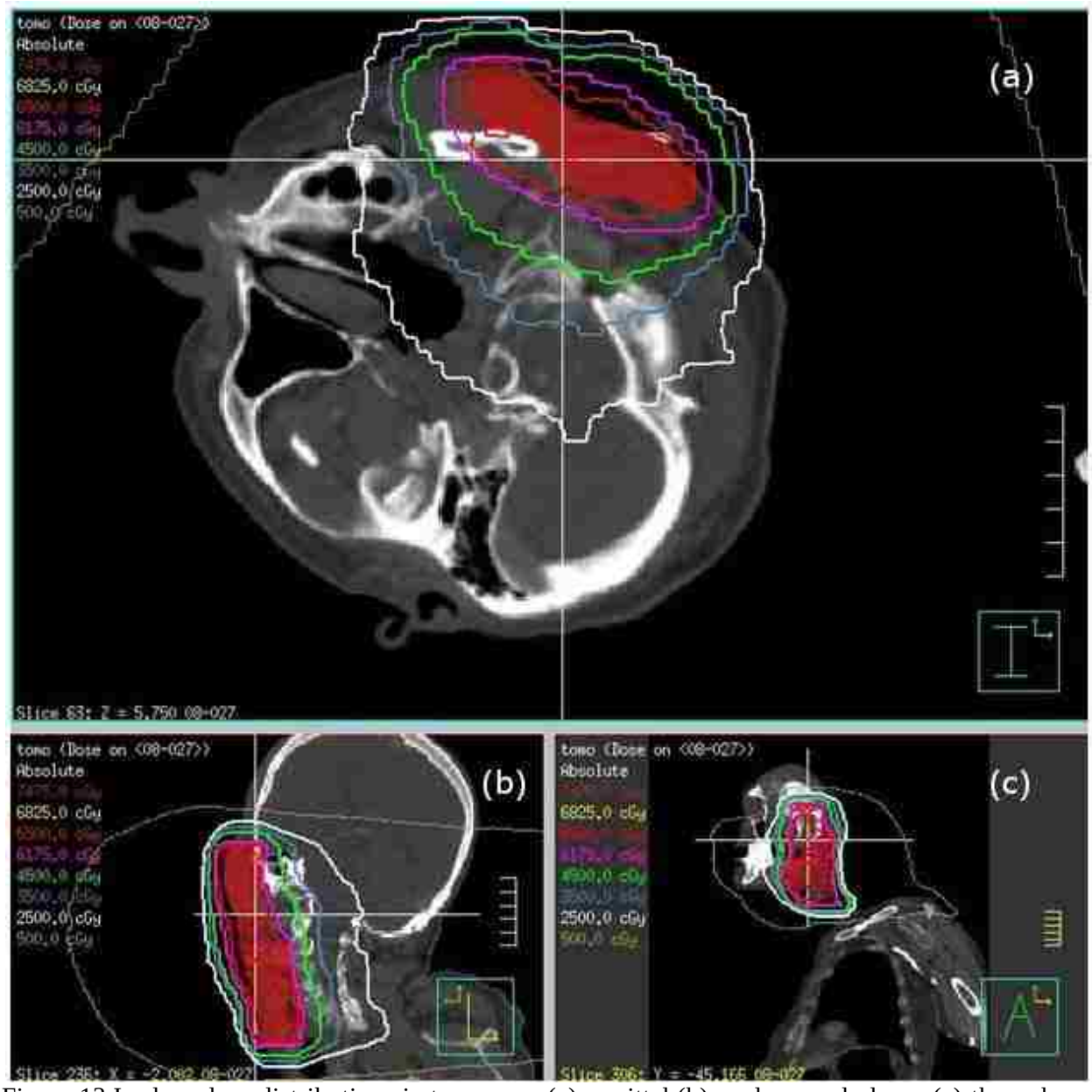

Figure 13 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 2 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash

3.3.2.1 HT

The HT isodose distribution showed a more conformal coverage of the PTV than the IMRT and mixed beam plans. No hotspots greater than 5% were seen in the HT plan.

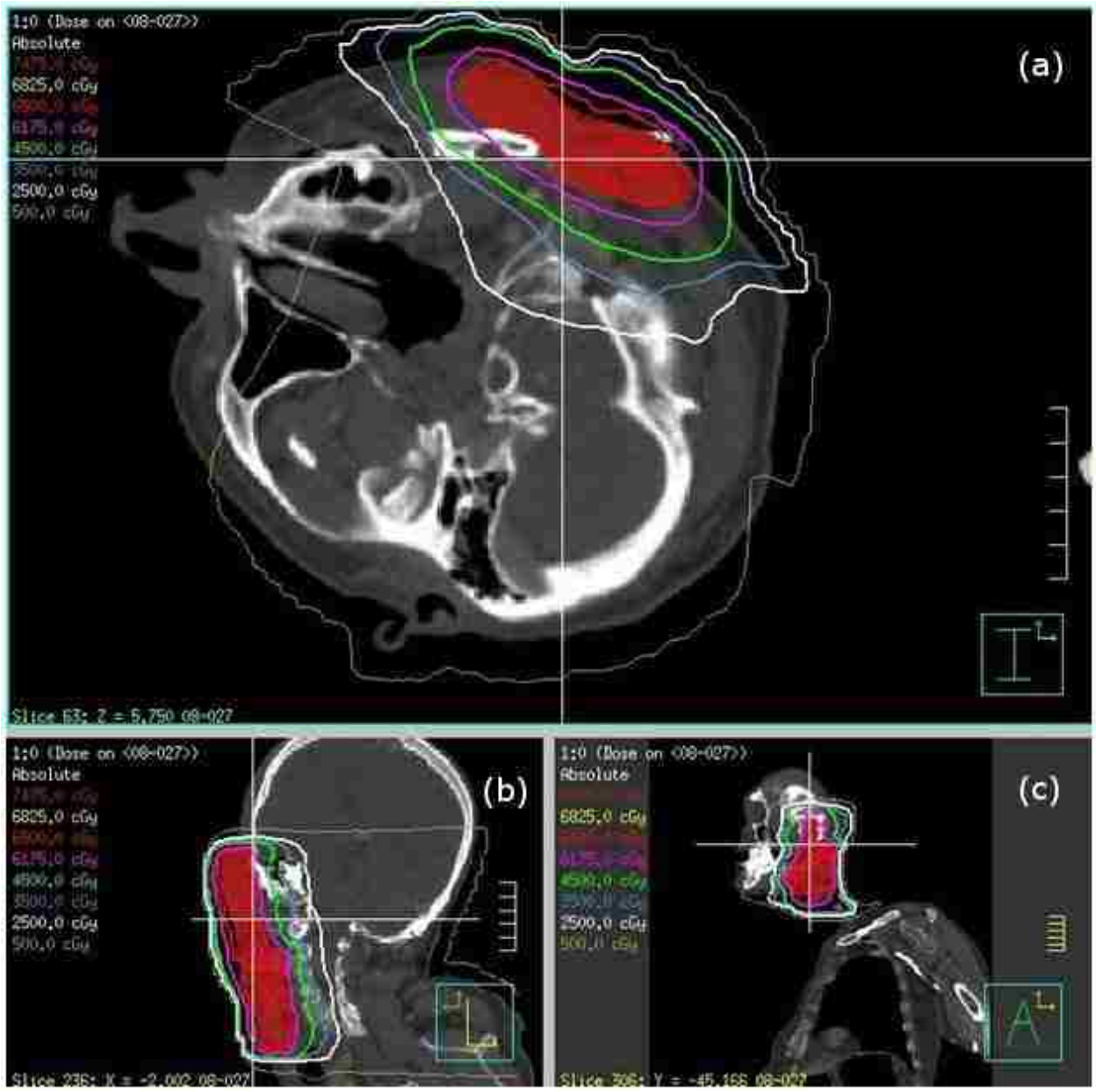

Figure 14 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 2 for the IMRT plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash

The red isodose line (the desired prescription dose) closely covers the PTV in comparison to the IMRT and mixed beam plans. The HT plan showed a slower distal fall off to the 45 Gy (green isodose line) than the IMRT or mixed beam plans. Also, the HT plan showed a larger area of normal tissue outside the PTV receiving a dose lower than 35 Gy compared to the IMRT and mixed beam plans.

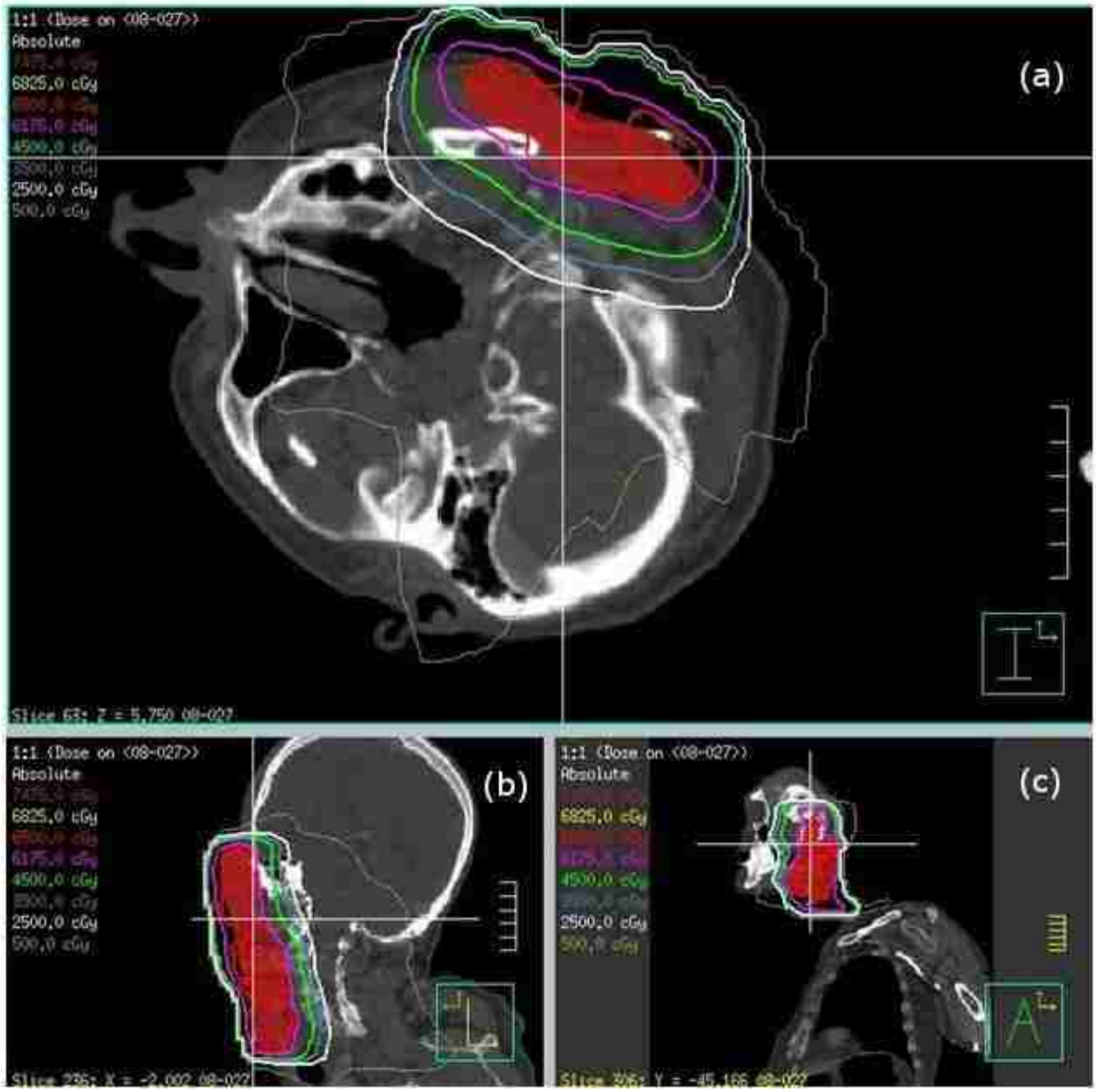

Figure 15 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 2 for the 1:1 ratio mixed beam plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash

3.3.2.2 IMRT/Mixed Beam

The IMRT (Figure 14) and the selected mixed beam isodose distributions (Figure 15 and Figure 16) showed less conformal PTV coverage than the HT but also displayed preferable features in the dose distribution.

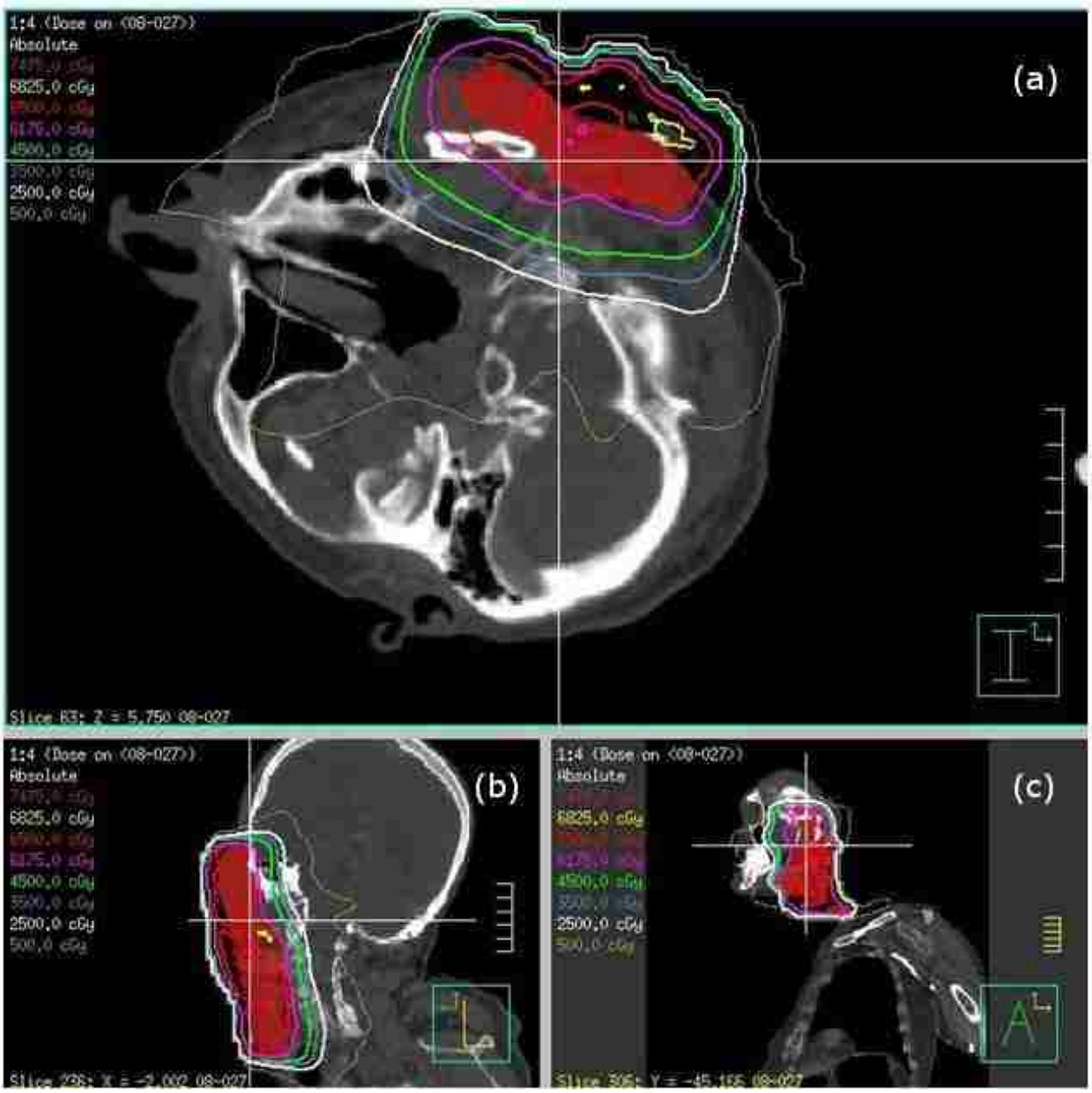

Figure 16 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 2 for the 1:4 ratio mixed beam plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash

The IMRT plan, in contrast to the HT plan, had a small (less than 5%) cold spot near the center of the PTV as seen the sagittal and coronal planes in Figure 14. The two selected mixed beam plans displayed larger inhomogeneities in the PTV than the HT or IMRT plans (with this being more evident in the 1:4 ratio mixed beam plan than the 1:1). For the 1:4 ratio mixed beam plan (Figure 16), a 5% hot spot is visible on the inferior section of the ear and a 5% cold spot near the center of the PTV.

The IMRT and mixed beam plan isodose distributions exhibited a sharper distal fall off compared to the HT plan and a lower dose near the eyes. Combining the electrons to the IMRT plan reduces the volume of tissue receiving a dose greater than 25 Gy and greatly reduces the tissue receiving a dose greater than 5 Gy. The 5 Gy isodose line can be seen encompassing the patient's cranium in the HT plan, nearly encompassing in the IMRT plan, however, the mixed beam plans encompass a much smaller volume of tissue.

3.3.3 DVH Comparisons

3.3.3.1 All mixed beam plans

DVH comparisons for the PTV and OARs for the mixed beam plans are shown in Figure 17 and Figure 18, respectively. The mixed beam plans all showed similar PTV dose volume coverage with the exception of the 0:1 ratio (electron only) plan, which was significantly larger volume receiving above and below the desired prescription.

For the OARs, there was a strong correlation between the amount of electrons in the mixed beam ratio and the OAR sparing. The 0:1 ratio plan gave the lowest max dose to the spinal cord and the lowest mean dose to the contralateral parotid, followed by the 1:4 ratio mixed beam plan. With the exception of the electron only plan, all mixed beam plans showed a similar dose-volume relationship for the ipsilateral eye. The spinal cord was well below the optimization constraint set of 45 Gy, yet, the mixed plan plans continually reduced the dose to the spinal cord as more electrons were introduced. A similar observation

can be made with the contralateral parotid. Depending on the physician's preference to spare the OARs at the expensive of PTV homogeneity both the 1:1 and 1:4 ratio plan give desirable DVH results.

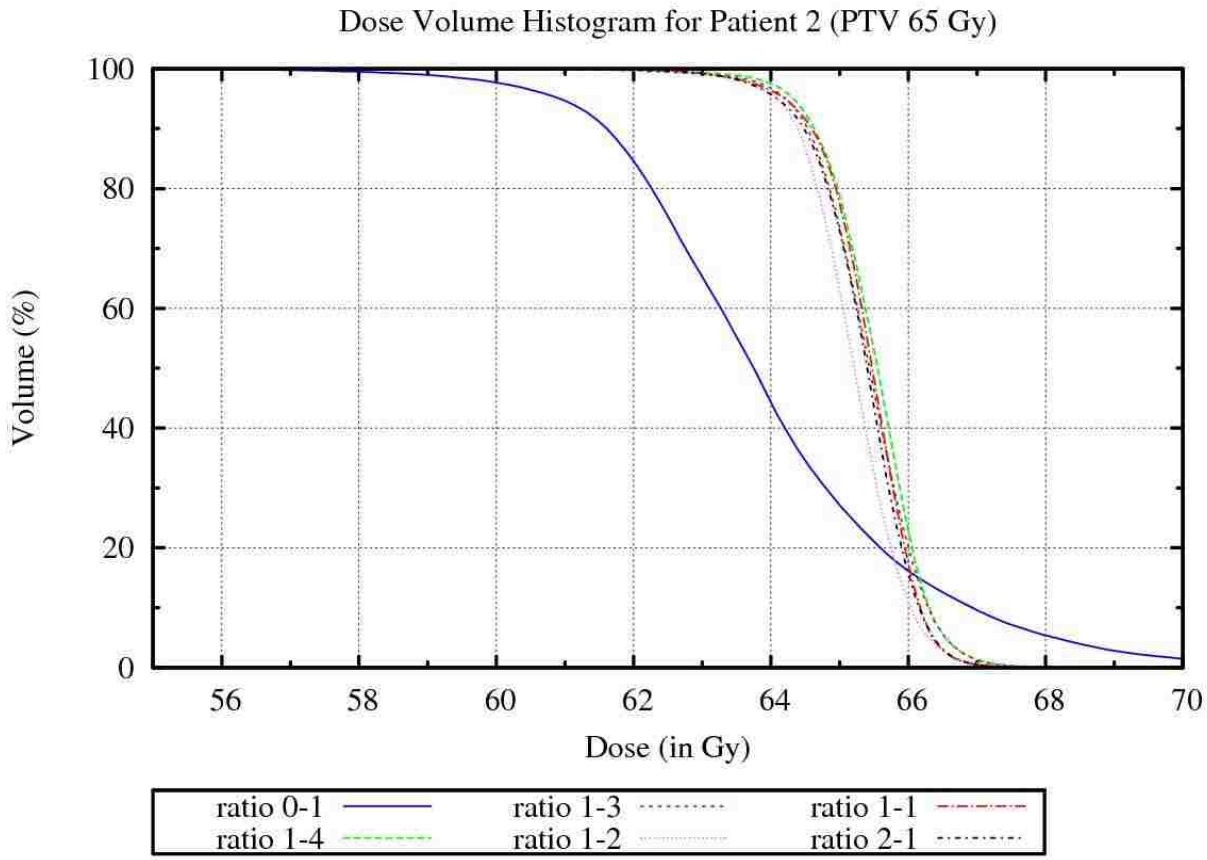

Figure 17 DVHs for patient 2 for the PTV of the mixed beam plans.

3.3.3.2 Select mixed beams, HT, and IMRT

DVHs for the PTV and OARs for the HT, IMRT, and selected mixed beams (1:1 and 1:4 ratio) are shown in Figure 19. The HT plan showed a smaller volume of PTV receiving greater than and less than the prescription dose of 65.0 Gy compared to the IMRT and mixed beam plans (this is reflected in the isodose distribution of Figure 13). The HT plan showed a more uniform dose distribution in the PTV.

For the OARs, the HT and IMRT plans had a similar maximum spinal cord dose. Introducing electrons to the plans reduced the maximum spinal cord dose in the 1:1 ratio and even more so for the 1:4

plan. The mixed beam plans had the contralateral parotid receive a lower mean dose than either the IMRT or HT plan. Overall, the mixed beam plans maintained the excellent sparing of the contralateral parotid that was exhibited in the electron only plan while at the same time restoring the PTV's DVH near that of the HT plan.

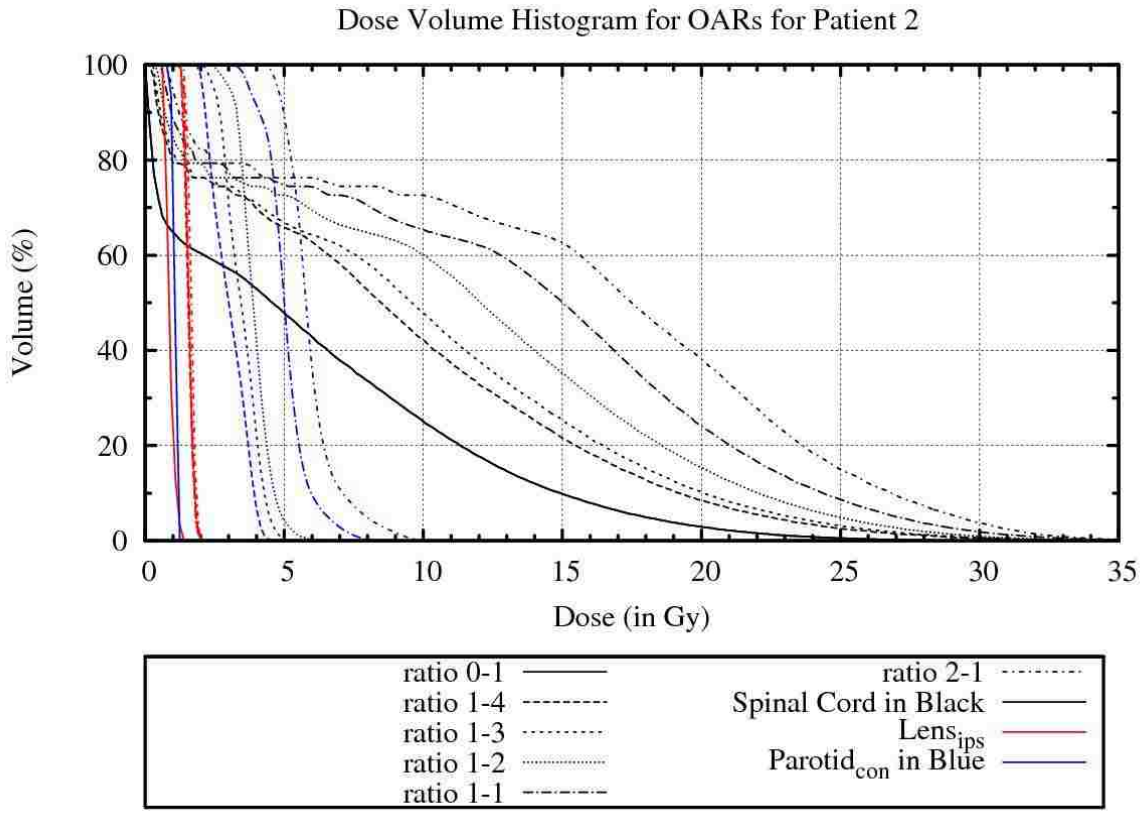

Figure 18 DVHs for patient 2 for the OARs of the mixed beam plans.

3.3.4 Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of the HT, IMRT, and mixed beam plans and found them to be clinically acceptable. A complete list of individual plan reviews can be found in Appendix A. After reviewing the dose distributions and DVHs for all the plans, he was indifferent on

how the HT plan compared to the mixed beam plan. The PTV coverage of the HT plan and the lower contralateral parotid dose of the mixed beam plan was the reason for being indifferent.

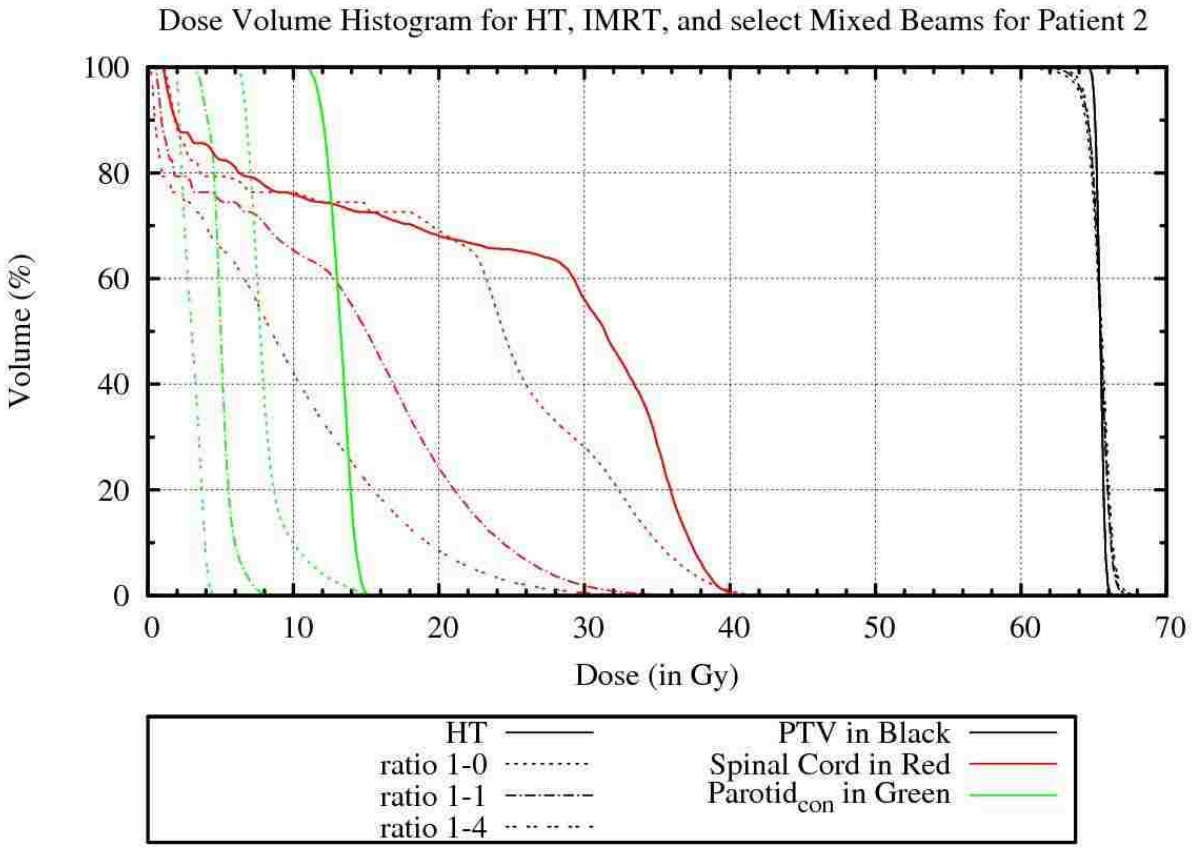

Figure 19 DVHs for patient 2 for the PTV and OARs for the HT, 1:0 ratio (IMRT), 1:1 ratio and 1:4 ratio mixed beam plan

3.3.5 Dose Statistics for the PTV and TCP

3.3.5.1 All mixed beam plans

Table 13 gives the dose statistics for the PTV from the mixed beam plans. The TCP values were high in all cases. The TCP model estimated nearly 100% tumor control for all the plans but the electron-only plan, which was 99.7% tumor control. CI was highest for 1:1 ratio plan (0.699) followed by the IMRT plan with 0.063. There was a weak correlation between the electron involvement and CI, however, the electron only plan greatly increases with the additional component of IMRT (going from 0.176 to

0.591 in the 1:4 ratio). Dose homogeneity index was similar for all mixed beam plans (within ± 0.002 of 0.055). Overall, the mixed beam plans are similar in dose statistics for the PTV.

Table 13 Dose statistics for the PTV for mixed beam plans for patient 2

PTV – Patient 2					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
1:0	100.0	0.650	0.063	66.8	62.7
2:1	100.0	0.654	0.055	66.8	63.2
1:1	100.0	0.699	0.054	66.8	63.3
1:2	100.0	0.520	0.057	66.8	63.1
1:3	100.0	0.596	0.057	66.9	63.2
1:4	100.0	0.591	0.053	67.0	63.5
0:1	99.7	0.176	0.177	70.6	59.1

3.3.5.2 Select mixed beams, HT, and IMRT plans

Table 14 gives the dose statistics for the PTV from the HT, IMRT, and select mixed beam plans. The TCP values were within ± 0.2% of 99.9% tumor control. The CI was highest for the HT plan (0.765) compared to the mixed beam plans (0.699 and 0.591 for the 1:1 and 1:4, respectively). The DHI value did not vary much between the two mixed beam plans (~0.053), however the DHI was significantly lower for the HT plan (0.017). The HT plan showed a lower DHI value, indicating the HT plan was more homogeneous over the PTV.

Table 14 Dose statistics for the PTV for the HT, IMRT, and select mixed beam plans

PTV- Patient 2					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
HT	99.9	0.765	0.017	66.0	64.9
1:0	100.0	0.650	0.063	66.8	62.7
1:1	100.0	0.699	0.054	66.8	63.3
1:4	100.0	0.591	0.053	67.0	63.5

3.3.6 Dose Statistics of the OARs and NTCP

Table 15 Dose statistics for the OARs for the mixed beam plans for patient 2

Critical Structures – Patient 2												
	$Parotid_{con}$		Spinal cord		$Lens_{con}$		$Lens_{ips}$		Eye_{con}	Eye_{ips}	optic $nerve_{con}$	optic $nerve_{ips}$
Plan	Dmean	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	Dmax	Dmax	Dmax
1:0	8.2	8.6	43.3	0.3	1.8	<0.1	2.2	<0.1	5.9	2.9	7.6	11.1
2:1	6.0	6.8	39.0	0.1	1.7	<0.1	2.1	<0.1	4.8	4.8	6.2	13.5
1:1	5.1	6.1	37.2	<0.1	1.8	<0.1	2.0	<0.1	3.8	5.0	4.7	13.7
1:2	4.0	5.3	36.1	<0.1	1.4	<0.1	2.0	<0.1	3.4	5.1	3.8	14.1
1:3	3.5	5.0	35.8	<0.1	1.4	<0.1	2.0	<0.1	2.9	5.6	3.0	14.0
1:4	3.1	4.8	35.6	<0.1	1.6	<0.1	2.1	<0.1	3.6	6.0	3.7	16.0
0:1	1.1	3.7	30.7	<0.1	0.5	<0.1	1.4	<0.1	0.9	5.7	1.6	14.6

Table 16 Dose statistics for the OARs for the HT, IMRT, and select mixed beam plans for patient 2

Critical Structures – Patient 2												
	$Parotid_{con}$		Spinal cord		$Lens_{con}$		$Lens_{ips}$		Eye_{con}	Eye_{ips}	Optic $nerve_{con}$	Optic $nerve_{ips}$
Plan	Dmean	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	Dmax	Dmax	Dmax
HT	13.2	14.4	41.2	0.4	3.1	0.1	3.4	0.1	12.0	11.9	16.5	21.4
1:0	8.2	8.6	43.3	0.3	1.8	<0.1	2.2	<0.1	5.9	2.9	7.6	11.1
1:1	5.1	6.1	37.2	<0.1	1.8	<0.1	2.0	<0.1	3.8	5.0	4.7	13.7
1:4	3.1	4.8	35.6	<0.1	1.6	<0.1	2.1	<0.1	3.6	6.0	3.7	16.0

3.3.6.1 Contralateral parotid

3.3.6.1.1 All mixed beam plans

Table 15 gives the dose statistics for the contralateral parotid for the mixed beam plans. Mean dose and NTCP of salivary flow reduction to less 25% at six weeks was computed. Mean dose values

had a strong correlation with electron involvement and ranged from 8.2 Gy for the 1:0 (IMRT only) to 1.1 Gy for the 0:1 (electron only). The NTCP followed the same trend as the mean dose. Using the 1:1 ratio of electrons and photons reduced the NTCP for the contralateral parotid gland by approximately 2.5% from the IMRT only plan.

3.3.6.1.2 Select mixed beams (1:4, 1:1), HT, and IMRT plan

Table 16 gives the dose statistics for the contralateral parotid for the HT, IMRT, and select mixed beam plans. Mean dose and NTCP of salivary flow reduction to less than 25% at six weeks was computed. Mean dose values were 13.2 Gy for HT, 8.2 Gy for IMRT, 5.1 Gy for the 1:1 mixed beam ratio, and 3.1 Gy for the 1:4 mixed beam ratio. The 1:4 ratio plan significantly reduced the mean dose to the contralateral parotid gland by 10.1 Gy compared to the HT plan. This resulted in an improvement of NTCP from 14.4% to 4.8%.

3.3.6.2 Spinal Cord

3.3.6.2.1 All mixed beam plans

Maximum dose and NTCP of necrosis/myelitis was computed. Maximum dose values ranged from 43.3 Gy for the 1:0 ratio to 30.7 Gy for the 0:1 ratio. NTCP for necrosis/myelitis was highest for the 1:0 plan (0.3%) and lowest for the 0:1 ratio plan (<0.1%). A substantial reduction was seen between the 1:0 (maximum dose of 43.3 Gy) and the 2:1 ratio (maximum dose of 39.0 Gy).

3.3.6.2.2 Select mixed beam (1:4), HT, and IMRT plan

Maximum dose and NTCP of necrosis/myelitis was computed. Maximum dose values ranged from 43.3 Gy for the IMRT plan to 35.6 Gy for the 1:4 ratio plan. The HT plan was 2.1 Gy lower in maximum dose for the spinal cord than the IMRT but 5.9 Gy higher than the 1:4 ratio's maximum dose.

The risk of spinal cord complication for the HT plan was 0.4 % for the HT plan compared to <0.1% for the 1:1 and <0.1% for the 1:4 ratio. Using mixed beam plans reduced the NTCP for the spinal cord.

3.3.6.3 Eyes, lens, and optic nerves

3.3.6.3.1 All mixed beam plans

Table 15 gives the dose statistics for the eyes, lens, and optic nerves for the mixed beam plans. Maximum dose was computed for these OARs along with NTCP of cataract requiring (surgical) intervention. The maximum dose and NTCP values for the contralateral and ipsilateral lens were similar with the electron only plan giving a slightly lower maximum dose to both the contralateral and ipsilateral lens. For the eyes and the optic nerve, there was a general trend of the dose decreasing for the contralateral OAR as electron involvement increased, however, the reverse was observed for the ipsilateral OAR. Doses for these OARs had near zero NTCP values to induce blindness.

3.3.6.3.2 Select mixed beams, HT, and IMRT plan

Table 16 gives the dose statistics for the eyes, lens, and optic nerves for the HT, IMRT, and select mixed beam plans. Maximum dose was computed for these OARs along with NTCP of cataract requiring (surgical) intervention. The maximum dose for the lens, eyes, and optic nerves was higher in the HT plan than IMRT or mixed beam plans. The NTCP values for the lens to develop a cataracts requiring surgical intervention was higher in the HT plan, however, the NTCP value was still very small (0.081 for the ipsilateral lens).

3.3.7 Non-specific Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 4052 cm^3 for the HT plan, 3428 cm^3 for the IMRT plan, and 1235 cm^3 for the mixed beam plan. The difference in volume

between the HT and the mixed beam plan was 2817 cm^3. Normalizing the volumes to the HT plan, the mixed beam plan gave 30% volume.

3.4 Patient Three - Parotid

3.4.1 Patient Specific Information

A 36 year old female was diagnosed to have high grade adenoidcystic carcinoma of the right parotid gland, stage T2N0M0. She underwent a parotidectomy (positive margins) and was referred for postoperative radiation therapy to treat the parotid bed and stylomastoid region. 63.9 Gy in 32 fractions was delivered by IMRT.

3.4.2 Isodose Distributions

Isodose distributions for HT, IMRT (1:0), and a selected mixed beam plan (1:1 ratio) are displayed in Figure 20-22. Dose statistics for the isodose distributions can be found in Table 18 and Table 20. The white lines in the CT images indicate the position of the orthogonal planes and the purple colorwash indicates the primary PTV. The red isodose line represents the desired prescription dose (63.9 Gy) to the primary PTV. PTV60 (teal colorwash) and PTV54 (yellow colorwash) are also displayed.

3.4.2.1 HT

The HT isodose distribution showed more conformal coverage in the primary PTV than the IMRT and mixed beam plans. No hot spots over 5% were observed in the primary PTV for the HT plan. Slight ~5% cold spots (purple isodose line) were located on the distal edge of the PTV along the occipital bone and at the abutment region between the primary PTV and the secondary PTV60 (colorwashed as teal in Figure 20). The HT plan showed a steep dose fall off to 45 Gy near the base of the brain and brainstem compared to the IMRT and mixed beam plans. This resulted in lower dose to the posterior and inferior

section of the brain. For the primary and secondary PTVs, the maximum target doses were noticeably lower in the HT than the select mixed beam or IMRT plan.

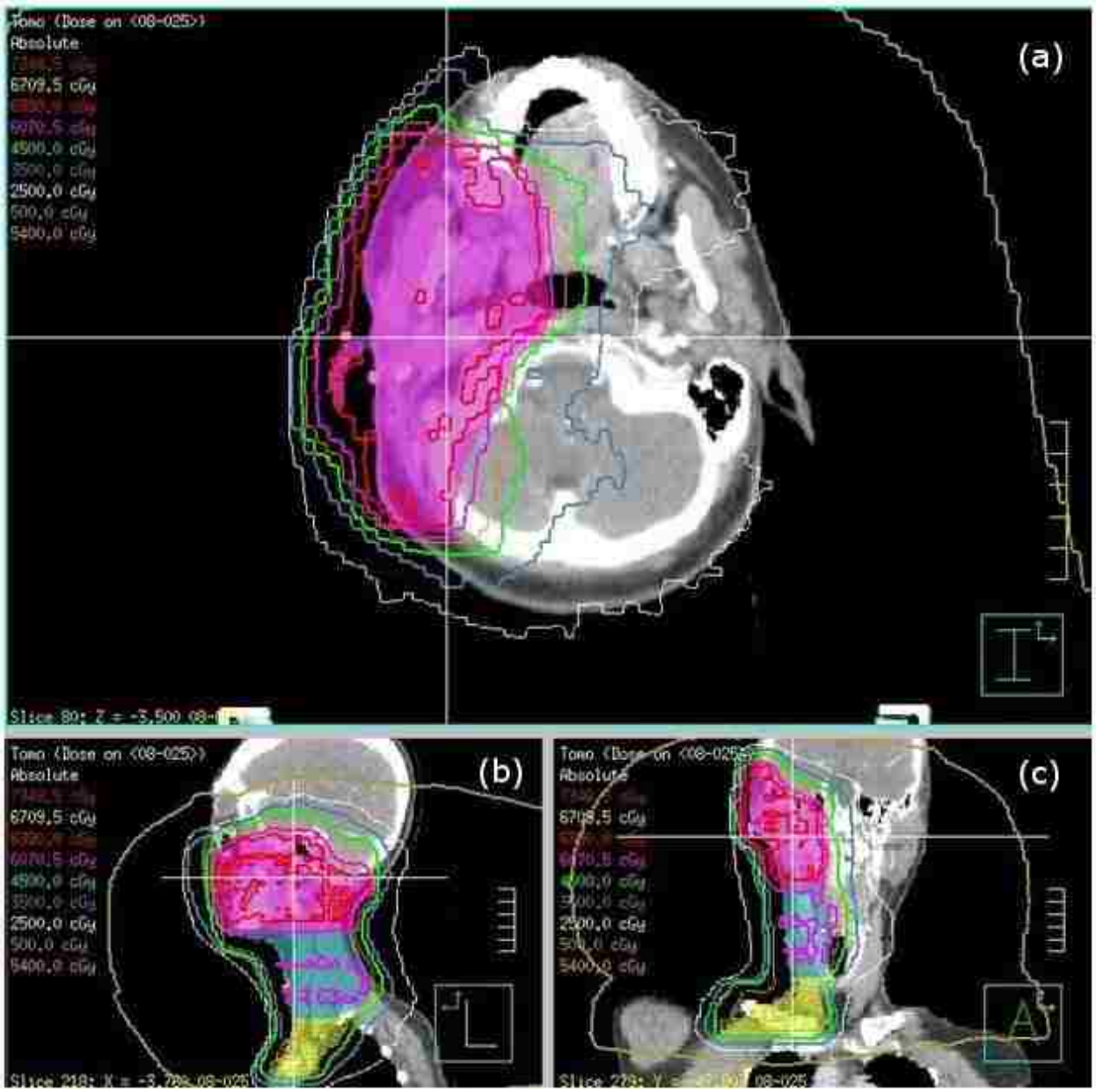

Figure 20 Isodose dose distribution in transverse (a), sagittal (b), and coronal planes (c) through the center of the primary PTV for patient 3 for TomoTherapy plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow.

3.4.2.2 IMRT/Mixed Beam

The IMRT and select mixed beam isodose distributions showed few hot and cold spots. 5% hot spots on the IMRT plan were located near the back of the neck on the primary PTV and posterior to the ipsilateral ear for the select mixed beam plan.

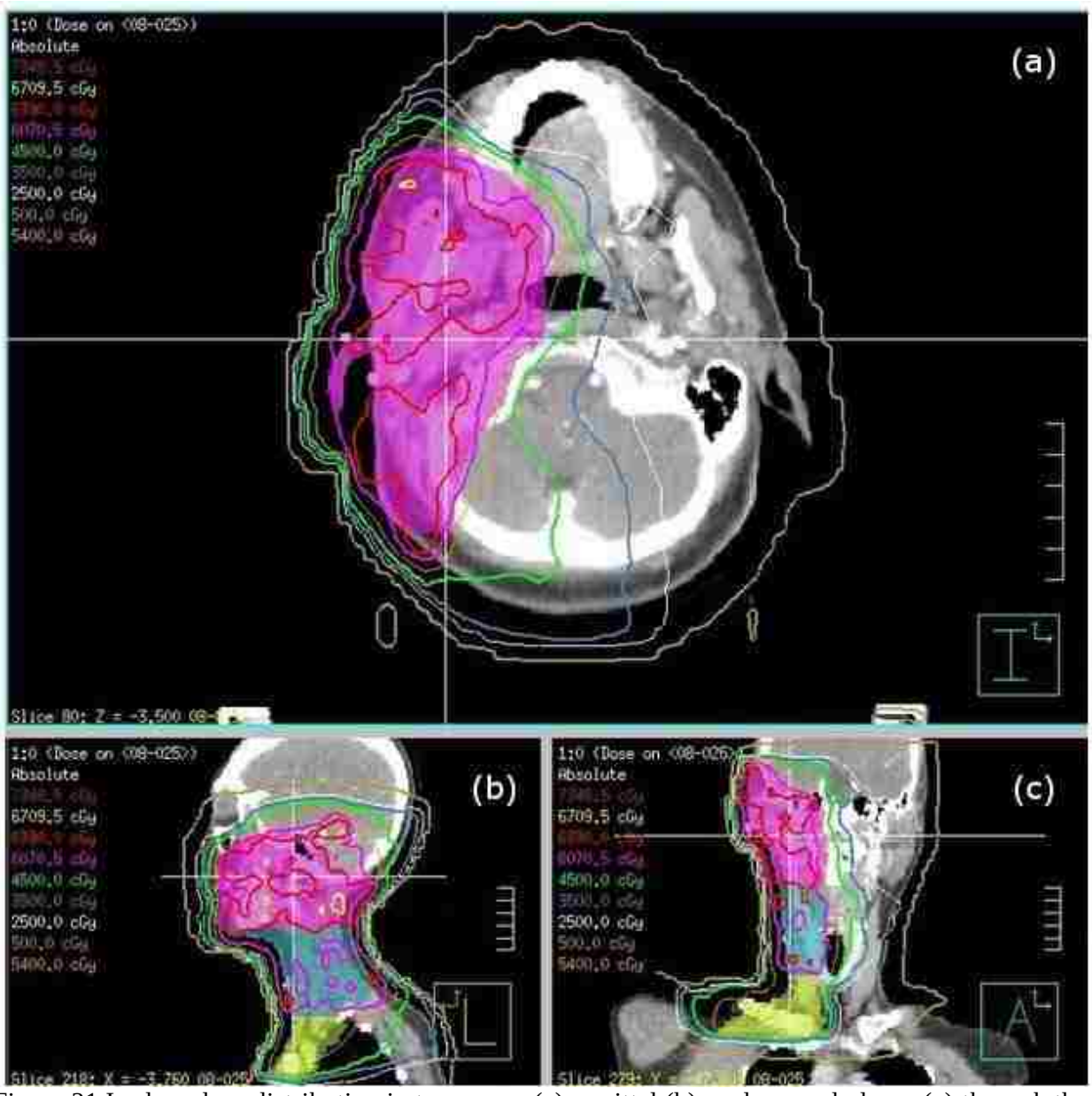

Figure 21 Isodose dose distribution in transverse (a), sagittal (b), and coronal planes (c) through the center of the primary PTV for patient 3 for IMRT (1:0) plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow.

Similar to the HT plan, 5% cold spots appeared near the junction of the primary and secondary PTV and also appeared near the near the region where the primary PTV abuts the brain.

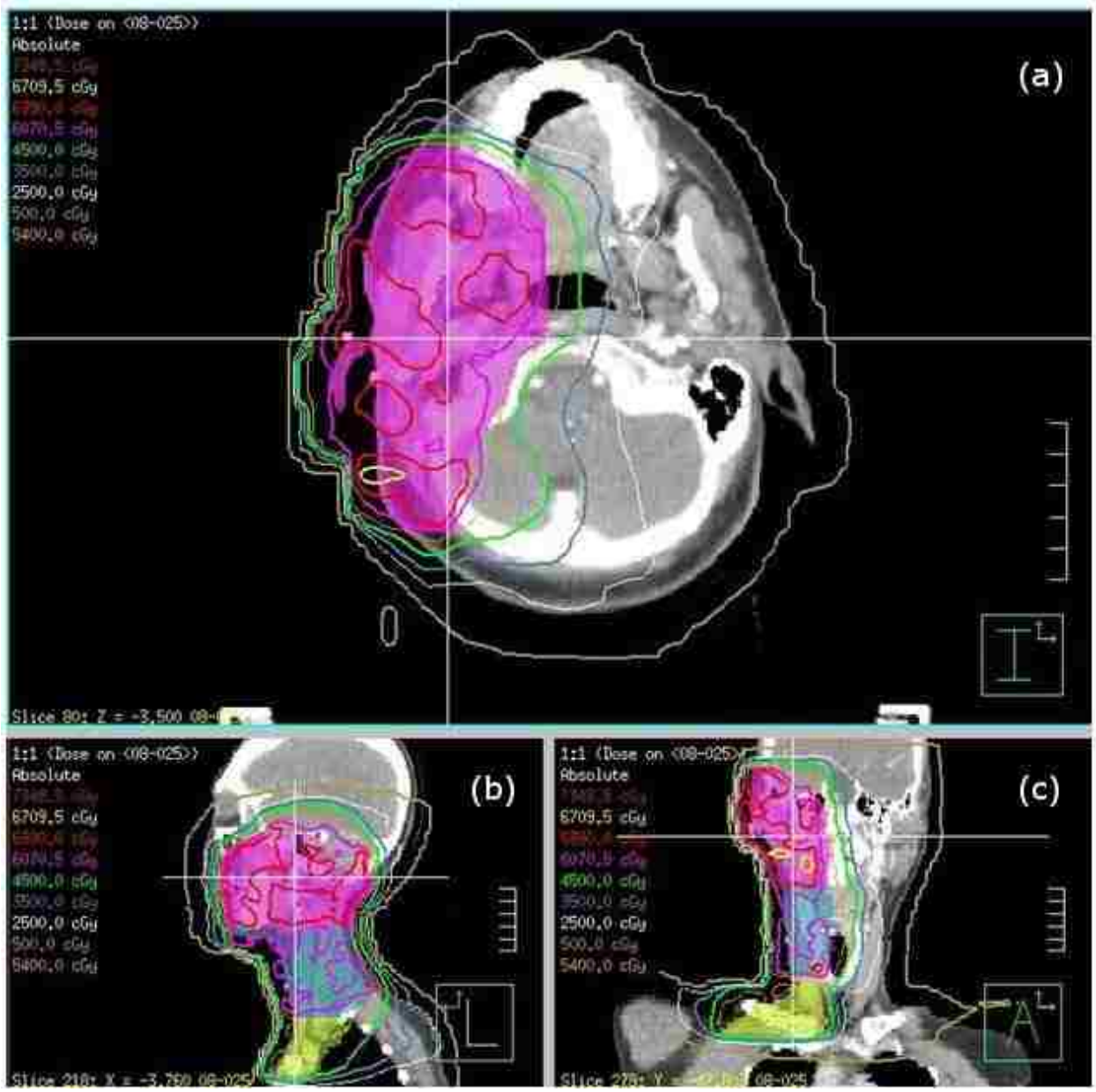

Figure 22 Isodose dose distribution in transverse (a), sagittal (b), and coronal planes (c) through the center of the primary PTV for patient 3 for the IMRT + electron (1:1) plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow.

The dose gradient for both IMRT and mixed beam plans at the distal edges of the targets was not as sharp as the HT plan. The green isodose line (45 Gy) shows the brain receiving more volume to a high dose.

The distal fall off to the 45 Gy isodose line is less for the mixed beam plan than the IMRT only. This is observable near the posterior region of the skull.

3.4.3 DVH Comparisons

3.4.3.1 All mixed beam plans

DVH comparisons for the PTV and OARs for the mixed beam plans are shown in Figure 23 and Figure 24, respectively.

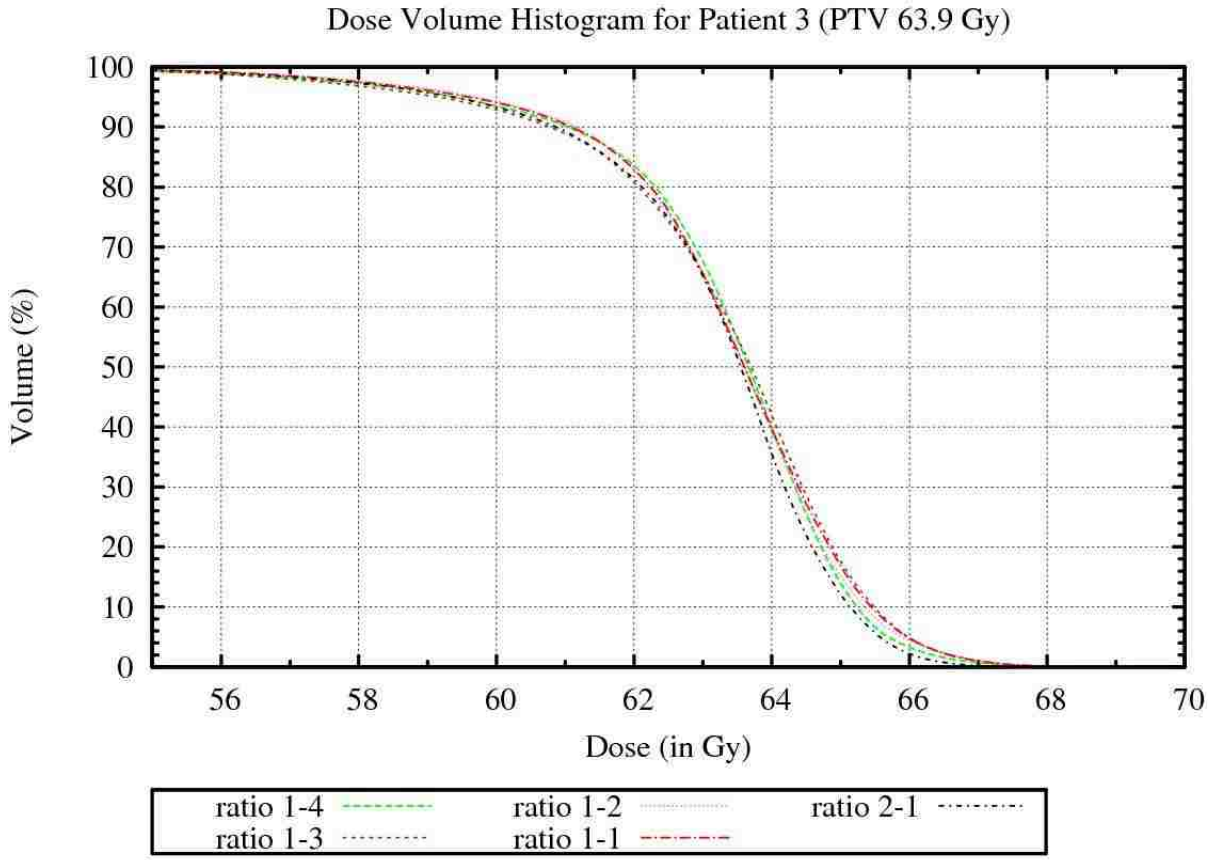

Figure 23 DVH for patient 3 for the PTV of the mixed beam plans

Note that the planning of the 0:1 electron only mixed beam plan was not performed for this patient because of the multiple PTV required abutting electron fields rather than a single enface electron beam.

The mixed beam plans all showed similar PTV dose volume coverage. Varying the electron involvement in the mixed beam plan did not contribute much changing the PTV coverage.

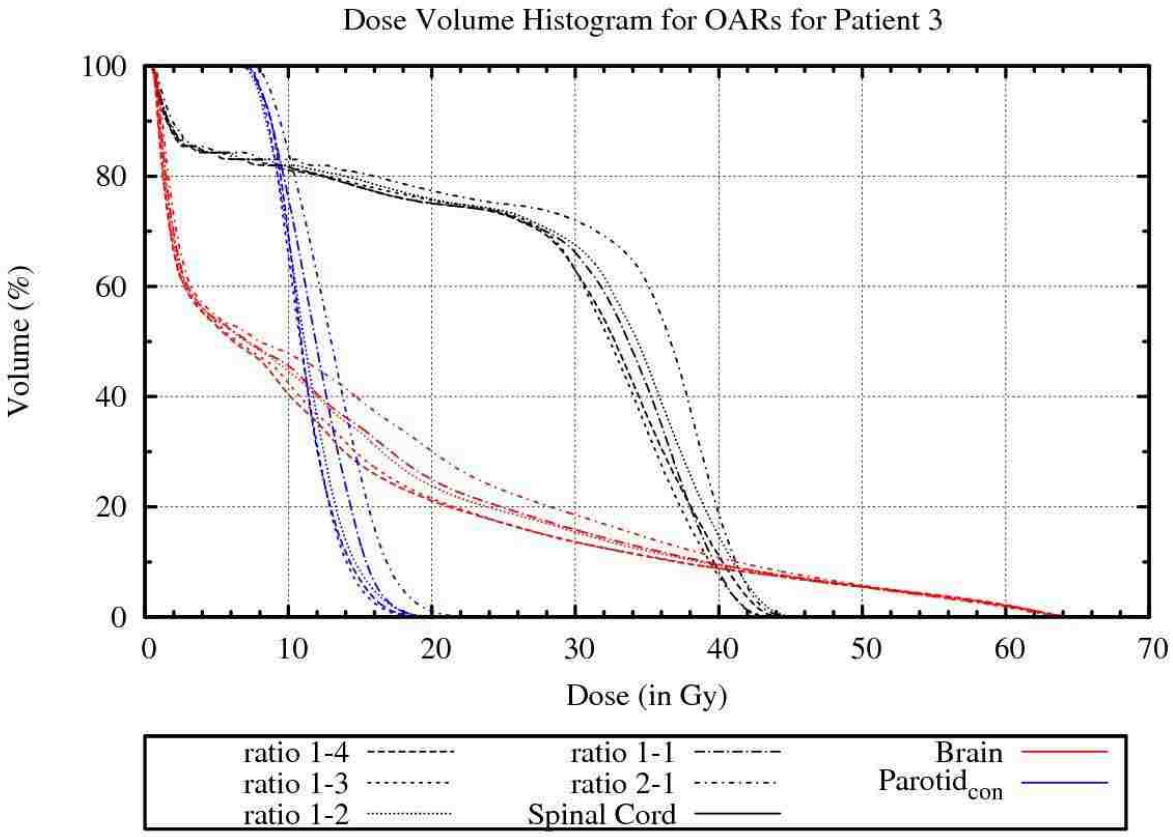

Figure 24 DVH for patient 3 for the OARs of the mixed beam plans

For the OARs, there was a general trend that the increasing the electron involvement reduced the mean dose for the contralateral parotid. This did not appear to be the case for the maximum dose to the spinal cord for which there was little correlation between. The volume of the brain receiving over 50 Gy was similar for the mixed beam plan, however separation between the plans appears between brain volume receiving 5 Gy and 40 Gy.

3.4.3.2 Select mixed beam, HT, and IMRT

DVHs for the PTVs for the HT, IMRT, and selected mixed beam (1:1 ratio) are shown in Figure 25 .

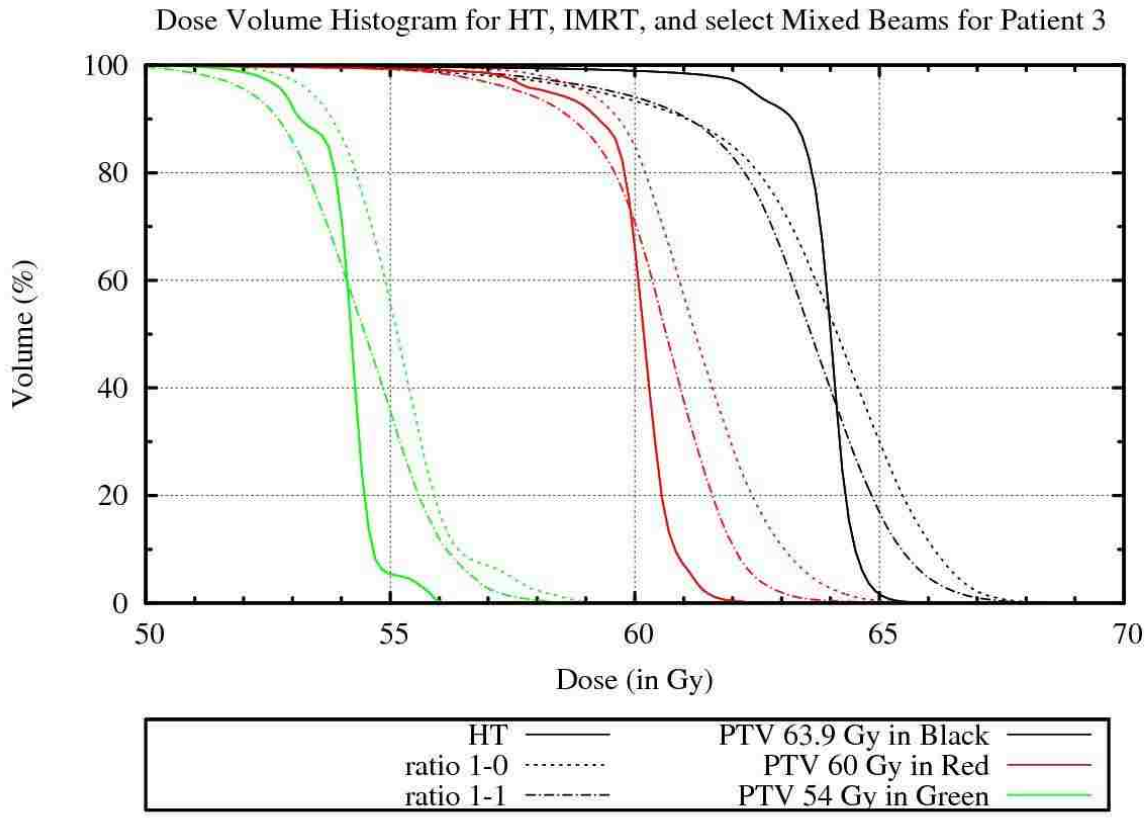

Figure 25 DVH for patient 3 for the PTV of the HT, IMRT, and selected mixed beam plan

The HT plan showed better dose homogeneity in the three PTVs. The mixed beam and IMRT plan showed small volumes of the PTV receiving lower than prescription dose which was created by the abutment of the PTVs and also the close proximity of the primary PTV to the spinal cord. The HT plan also showed the secondary PTVs receiving a smaller volume of dose pass the maximum prescription the respective PTV.

DVHs for the OARs for the HT, IMRT, and selected mixed beam are shown in Figure 26. The HT plan showed the lowest maximum spinal cord dose, along with the lowest volume of brain tissue receiving over 50 Gy. The IMRT and mixed beam plan gave similar volume of brain over 50 Gy. The mixed beam plan gave the lowest mean dose to the contralateral parotid.

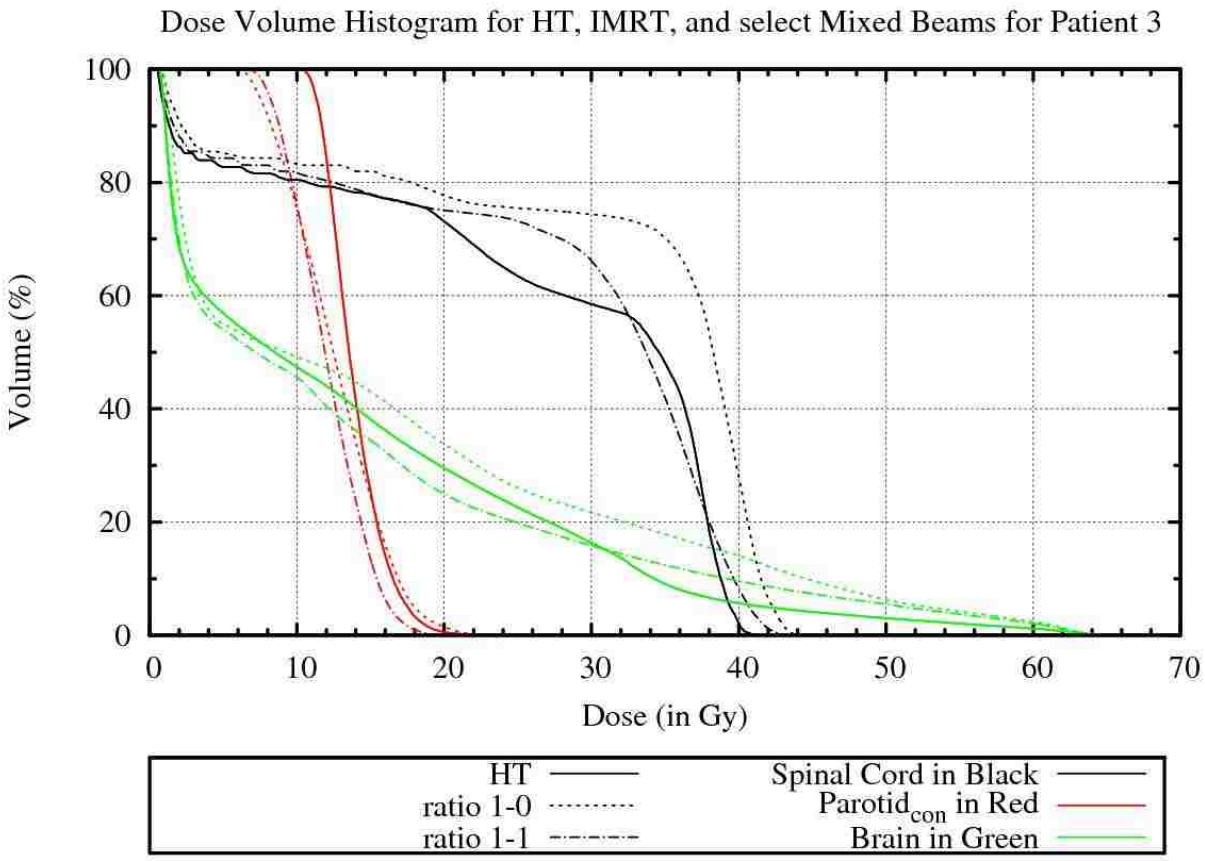

Figure 26 DVH for patient 3 for the OARs of the mixed beam plan

3.4.4 Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of the HT, IMRT, and mixed beam plans and found the HT plan to be marginally acceptable and was indifferent about the IMRT plan and the best mixed beam ratio. A complete list of individual plan reviews can be found in Appendix A. After reviewing the dose distributions and DVHs for all the plans, he ranked the HT plan superior to the mixed beam plan. Significant improvements in the PTVs coverage was listed as a reason for preferring HT plan over the mixed beam. The radiation oncologist suggested that the higher maximum dose to the spinal cord may be of concern.

3.4.5 Dose Statistics of the PTVs and TCP

3.4.5.1 All mixed beam plans

Table 17 gives the dose statistics for the PTV for the mixed beam plans. The TCP value for the primary PTV ranged from 99.0% for the 1:1 ratio plan to 97.7% for the 1:3 ratio plan. There did not appear too much correlation with heavier electron weighting and primary PTV's TCP. However, for the secondary PTVs, the IMRT plan gave higher TCP values and the TCP generally decreased with more electron involvement. CI was highest for the IMRT plan for all three PTVs. DHI was similar for all mixed beam plans, expect for the IMRT plan which had higher DHI values on the primary PTV and PTV54.

Table 17 Dose statistics for the PTV for the mixed beam plans for patient 3

PTV – Patient 3						
Patient 3	Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
PTV 63.9	1:0	98.7	0.517	0.186	67.4	55.5
	2:1	98.9	0.400	0.158	66.3	56.2
	1:1	99.0	0.412	0.166	67.0	56.4
	1:2	98.8	0.417	0.162	66.9	56.5
	1:3	97.7	0.413	0.176	66.9	55.7
	1:4	98.1	0.412	0.171	66.7	55.8
PTV 60	1:0	99.1	0.257	0.117	64.5	57.4
	2:1	98.6	0.197	0.128	63.4	55.7
	1:1	98.6	0.200	0.128	63.3	55.6
	1:2	98.4	0.184	0.147	63.9	55.0
	1:3	98.2	0.190	0.159	64.0	54.4
	1:4	98.1	0.203	0.158	63.7	54.3
PTV 54	1:0	92.7	0.094	0.112	58.5	52.5
	2:1	88.9	0.047	0.097	56.7	51.5
	1:1	89.0	0.052	0.126	57.5	50.7
	1:2	88.9	0.063	0.124	57.0	50.3
	1:3	89.8	0.063	0.108	57.2	51.3
	1:4	89.1	0.066	0.120	57.1	50.6

Table 18 Dose statistics for the PTV for the HT, IMRT, and select mixed beam plan

PTV – Patient 3						
patient 3	Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
PTV 63.9	HT	98.8	0.533	0.081	65.1	59.9
	1:0	98.7	0.517	0.186	67.4	55.5
	1:1	98.9	0.412	0.166	67.0	56.4
PTV 60	HT	97.9	0.166	0.091	61.6	56.2
	1:0	99.1	0.257	0.117	64.5	57.4
	1:1	98.6	0.200	0.128	63.3	55.6
PTV 54	HT	89.2	0.068	0.071	55.8	52.0
	1:0	92.7	0.094	0.112	58.5	52.5
	1:1	89.0	0.052	0.126	57.5	50.7

3.4.5.2 Select mixed beam, HT, and IMRT plans

Table 18 gives the dose statistics for the PTV from the HT, IMRT, and select mixed beam plan (1:1 ratio). TCP values for the primary PTV were similar with ± 0.2% of 98.8%. For the secondary PTVs, the IMRT plan resulted in the highest TCP. This higher TCP could be due to the high maximum dose of the IMRT plan. CI was highest for the HT plan (0.533) for the primary PTV. For the secondary PTVs, the IMRT only plan gave the highest CI values (PTV60=0.257 and PTV54=0.094). The HT plan showed the lowest DHI values, indicating that the HT plan was more homogeneous over the three PTVs.

3.4.6 Dose Statistics of the OARs and NTCPs

3.4.6.1 Contralateral parotid

3.4.6.1.1 All mixed beam plans

Table 19 gives the dose statistics for the contralateral parotid for the mixed beam plans. Mean dose and NTCP of salivary flow reduction to less than 25% at six weeks was computed. Mean dose

values ranged from 11.2 Gy for the 1:3 ratio plan to 13.2 Gy for the 2:1 ratio plan. This corresponded to NTCP values ranging from 11.8% to 14.3% for the 1:3 and 2:1, respectively.

3.4.6.1.2 Select mixed beam (1:1), HT, and IMRT plan

Table 20 gives the dose statistics for the contralateral parotid for the HT, IMRT, and select mixed beam plans. Mean dose was slightly higher for the HT plan (13.9 Gy) compared to the IMRT (12.6 Gy) and mixed beam plan (12.1 Gy). The NTCP values were as following: HT=15.4, IMRT=13.6 and 1:1 ratio=13.0.

3.4.6.2 Spinal Cord

3.4.6.2.1 All mixed beam plans

Maximum dose and NTCP of necrosis/myelitis was computed. The close proximity of the PTVs to the spinal cord resulted in larger than typically acceptable (45 Gy at our clinic) maximum spinal cord doses. The maximum spinal cord dose for the IMRT, 2:1, and 1:2 plan were slightly over the 45 Gy mark, with the largest being the 2:1 ratio (46.5 Gy). However comparing the NTCP values for the plans, the IMRT had the highest value at approximately 1% complication risk.

3.4.6.2.2 Select mixed beam (1:1), HT, and IMRT plan

Again the close proximity of the PTVs to the spinal cord resulted in larger than typically acceptable (45 Gy at our clinic) maximum spinal cord doses for the IMRT plan. Introducing a 1:1 ratio of electrons reduced the maximum spinal cord dose to 44.3 Gy. The lowest maximum spinal cord dose was the HT plan (41.3 Gy). However comparing the NTCP values for the plans, the IMRT had the highest value at approximately 1% complication risk.

3.4.6.3 Brain

3.4.6.3.1 All mixed beam plans

Maximum dose and NTCP of necrosis was computed for the brain. The heavier weighed electron ratio plans gave a higher maximum dose to the brain (69.3), however this was a small volume receiving the higher dose and NTCP values did not reflected the maximum dose trend. The highest NTCP value for the brain was the IMRT plan (0.1%) while the lowest value was the 1:3 ratio at (<0.1%).

3.4.6.3.2 Select mixed beam, HT, and IMRT plan

Maximum dose and NTCP of necrosis was computed for the brain. The IMRT and mixed beam plan has similar maximum dose values of about 67 Gy, however the IMRT plan showed an increase risk of complication (0.1 % for IMRT compared to <0.1% for the 1:1 ratio). The HT plan had a similar low risk of complication for the brain at about <0.1%.

3.4.6.4 Lens, eyes, optic chiasm, and optic nerve

3.4.6.4.1 All mixed beam plans

Maximum dose was computed for the lens, eyes, optic chiasm, and optic nerve along with NTCP values for cataracts requiring (surgical) intervention. The maximum dose and NTCP values for the contralateral lens increased with electron involvement in the ratio, going from 3.9 Gy with a 0.1% risk of complication for the IMRT plan to 5.4 Gy with a 0.3% risk for the 1:4 ratio plan. For the ipsilateral lens, the converse was true, and the IMRT gave the highest dose (7.0 Gy) and highest NTCP value (0.8). Below 1:2 ratio there was not much change in maximum dose for ipsilateral eye. The maximum dose for the eyes followed the same trend as the lens, with IMRT being the lowest contralateral maximum dose (6.3 Gy) and the highest ipsilateral dose (13.0 Gy). The maximum dose to the optic chiasm ranged from

45.6 Gy for the 1:1 ratio plan to 48.9 Gy for the 1:4 ratio plan. For the ipsilateral optic nerve, the maximum dose was 39.9 Gy for the 1:4 ratio and 32.7 Gy for the IMRT plan.

3.4.6.4.2 Select mixed beam, HT, and IMRT plan

Maximum dose to the lens and eyes was higher in the HT plan than the IMRT or select mixed beam plan. However, NTCP values were only slightly increased for the contralateral lens (0.6% compared to 0.1% for IMRT) and actually decreased for the ipsilateral lens (0.5% compared to 0.8% for IMRT). This is due to only a small volume being irradiated to the maximum dose. The maximum dose for the optic chiasm was lowest for the HT plan (36.6 Gy) and the maximum dose to the optic nerve was comparable to the other plans (33.4 Gy for HT).

Table 19 Dose statistics for the OARs for the mixed beam plans for patient 3

Critical Structures – Patient 3														
	$Parotid_{con}$		Spinal cord		$Lens_{con}$		$Lens_{ips}$		Brain		Eye_{con}	Eye_{ips}	Optic chiasm	Optic $nerve_{ips}$
Plan	Dmean	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax			
1:0	12.6	13.6	46.2	1.0	3.9	0.1	7.0	0.8	67.0	0.1	6.3	13.0	47.6	32.7
2:1	13.2	14.3	46.5	0.9	4.1	0.1	6.1	0.5	66.8	0.1	6.7	10.7	48.6	34.0
1:1	12.1	13.0	44.3	0.6	4.6	0.2	6.0	0.4	67.1	0.1	7.7	10.3	45.6	35.4
1:2	11.5	12.1	46.0	0.9	4.9	0.2	5.6	0.4	68.4	0.1	8.2	10.1	47.9	37.2
1:3	11.2	11.8	44.4	0.6	5.2	0.3	5.7	0.4	68.1	<0.1	8.6	10.2	47.3	34.8
1:4	11.3	12.0	45.2	0.7	5.4	0.3	5.7	0.4	69.3	0.1	9.0	10.3	48.9	39.9

3.4.7 Non-specific Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 3004 cm^3 for the HT plan, 2285 cm^3 for the IMRT plan, and 2640 cm^3 for the mixed beam plan. The difference in volume between the HT and the mixed beam plan was 364 cm^3. Normalizing the volumes to the HT plan, the mixed beam plan gave 88% volume.

Table 20 Dose statistics for the OARs for the HT, IMRT, and select mixed beam for patient 3

Critical Structures – Patient 3														
	$Parotid_{con}$		Spinal cord		$Lens_{con}$		$Lens_{ips}$		Brain		Eye_{con}	Eye_{ips}	Optic chiasm	Optic $nerve_{ips}$
Plan	Dmean	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax	NTCP	Dmax			
HT	13.9	15.4	41.3	0.5	7.6	0.6	7.4	0.5	65.2	<0.1	18.3	25.4	36.6	33.4
1:0	12.6	13.6	46.2	1.0	3.9	0.1	7.0	0.8	67.0	0.1	6.3	13.0	47.6	32.7
1:1	12.1	13.0	44.3	0.6	4.6	0.2	6.0	0.4	67.1	<0.1	7.7	10.3	45.6	35.4

3.5 Patient Four – Nasal Cavity

3.5.1 Patient Specific Information

A 73 year old male was diagnosed to have moderately differentiated squamous cell carcinoma in the left nasal cavity, stage T1-2N0M0. Radiation was used as a definitive treatment of his lesion. He received 70 Gy at 2 Gy per fraction with IMRT.

3.5.2 Isodose Distributions

Isodose distributions for HT, IMRT, and the selected mixed beam plan (1:3 ratio) are displayed in Figure 27-29. Dose statistics for the isodose distributions can be found in Table 22 for the PTV and Table 24 for the critical structures. The white lines in the CT images indicate the position of the orthogonal planes and the red colorwash indicates the primary PTV. The red isodose line represents the desired prescription dose (70.0 Gy) to the PTV.

3.5.2.1 HT

The HT isodose distribution showed a conformal coverage with fewer cold spots than the IMRT and mixed beam plans for the PTV. Hot spots in the HT plan were small (~5%) and were generally

located along the surface of the nose. These 5% hotspots (73.5 Gy) observable in the yellow isodose line can be seen in Figure 27.

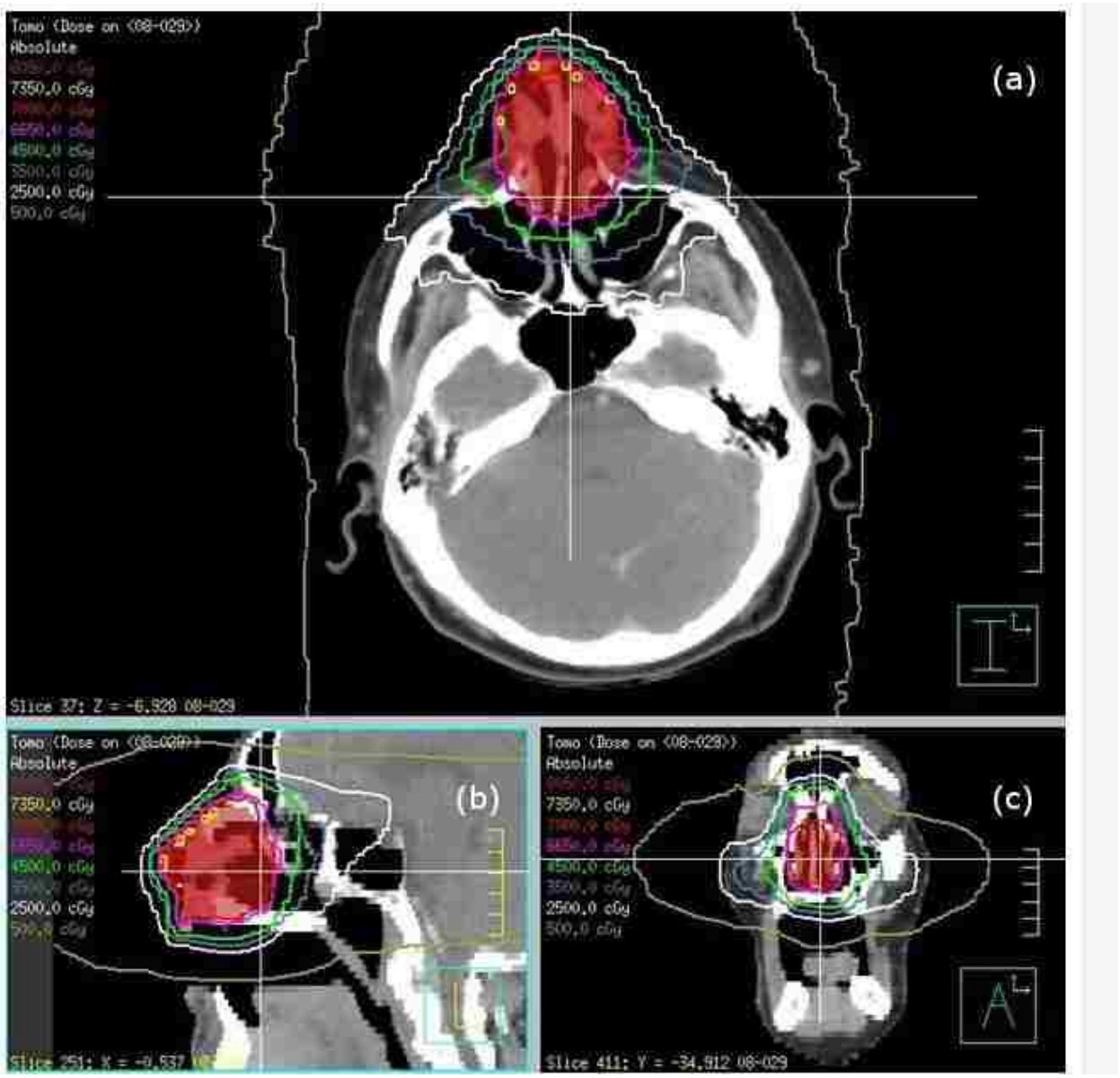

Figure 27 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 4 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

No cold spots greater than 5% were noted in the PTV for the HT plan. The HT plan showed a steep dose fall off on distal edge of the PTV. For the HT plan, a significant volume of tissue outside the PTV received low dose (5 Gy or more) compared to the mixed beam plan.

3.5.2.2 IMRT/Mixed Beam

The IMRT and the select mixed beam plan isodose distributions showed less conformal PTV coverage, slower high dose fall off at the distal PTV edge, but lower volumes of tissue receiving over 5 Gy.

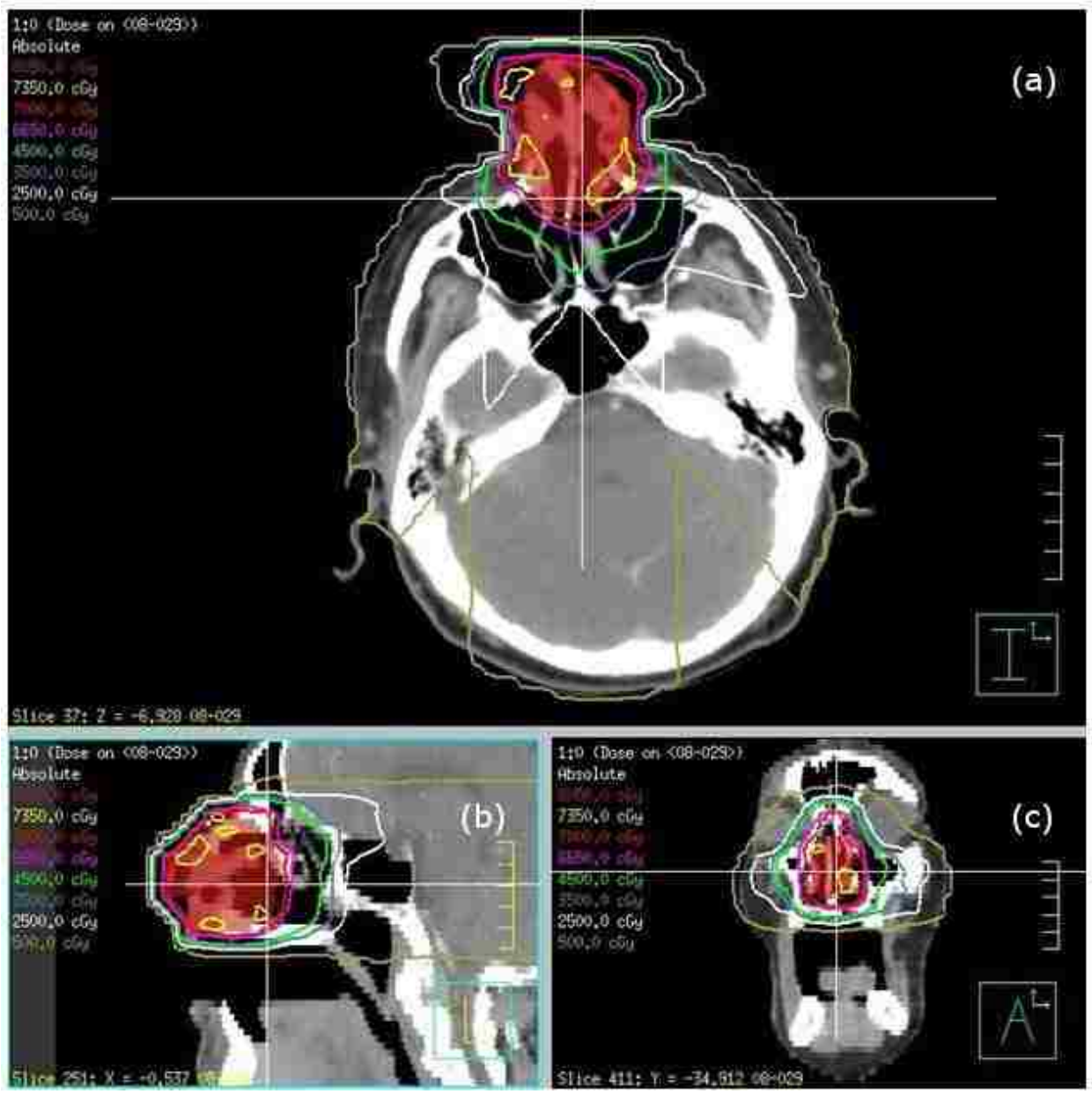

Figure 28 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 4 for the IMRT (1:0) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

5% hotspots appear in the IMRT along the posterior edge of the PTV and along the bridge of the nose. This can be seen in the sagittal slice in Figure 28. The mixed beam plan is slightly less conformal than the IMRT plan. Larger volumes of PTV had 5% hotspots that were located near the center of the PTV, which is possibly due to electron scatter in the nasal passages.

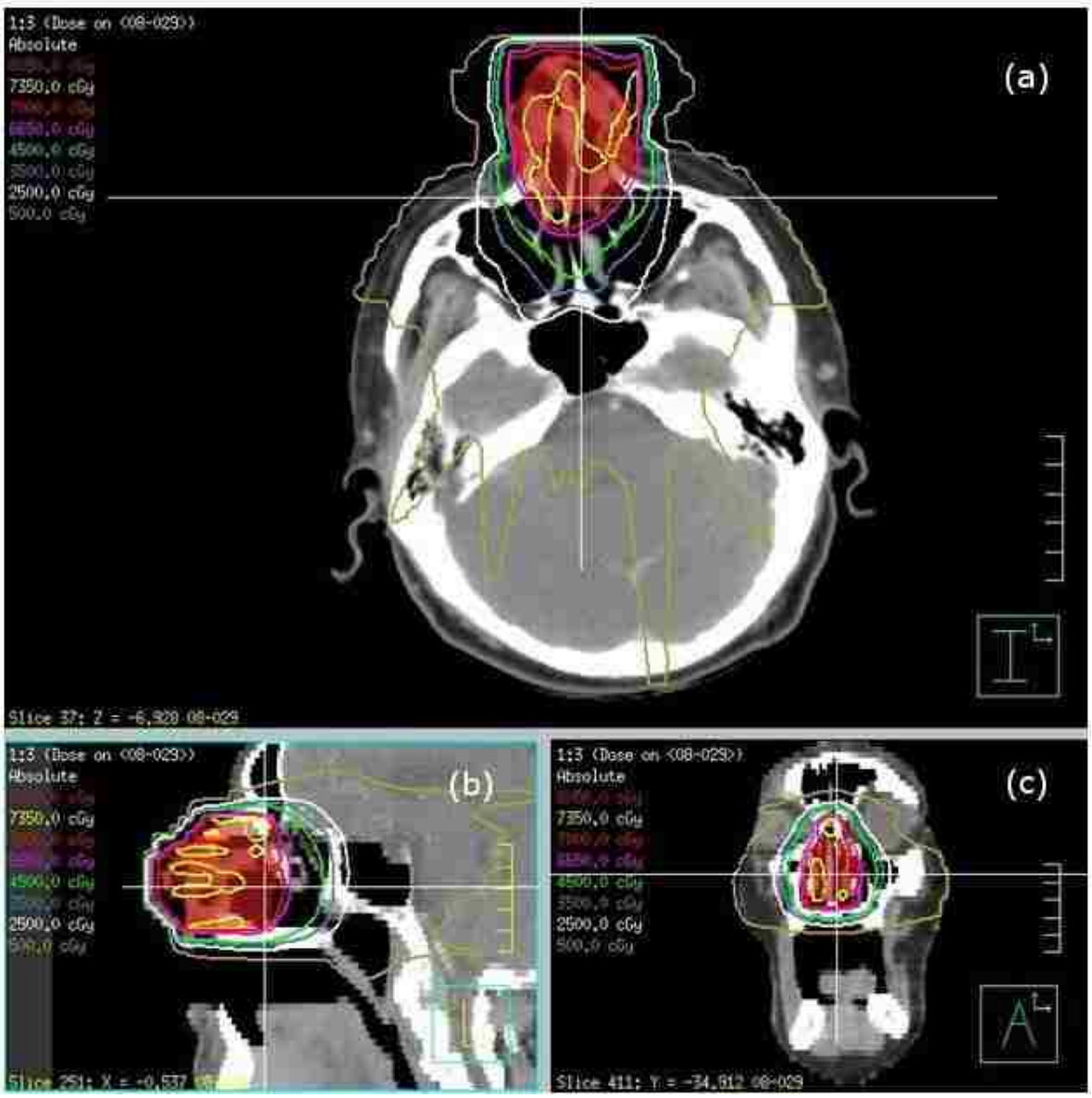

Figure 29 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 4 for the IMRT + electron (1:3) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The dose fall off to 45 Gy (the green isodose line) is faster in the HT plan and falls off distally before the sphenoid bone as where 45 Gy isodose line just touches the sphenoid bone in the mixed beam and IMRT plan, as seen in the sagittal slices. The amount of tissue receiving over 5 Gy is noticeably less in the mixed beam plan compared to the HT plan and IMRT plan.

3.5.3 DVH Comparisons

3.5.3.1 All mixed beam plans

DVH comparisons for the PTV and OARs for the mixed beam plans are shown in Figure 30 and Figure 31, respectively. The mixed beam plans all showed similar PTV does volume coverage with the exception of the 0:1 ratio (electron only) plan, which was significantly less conformal.

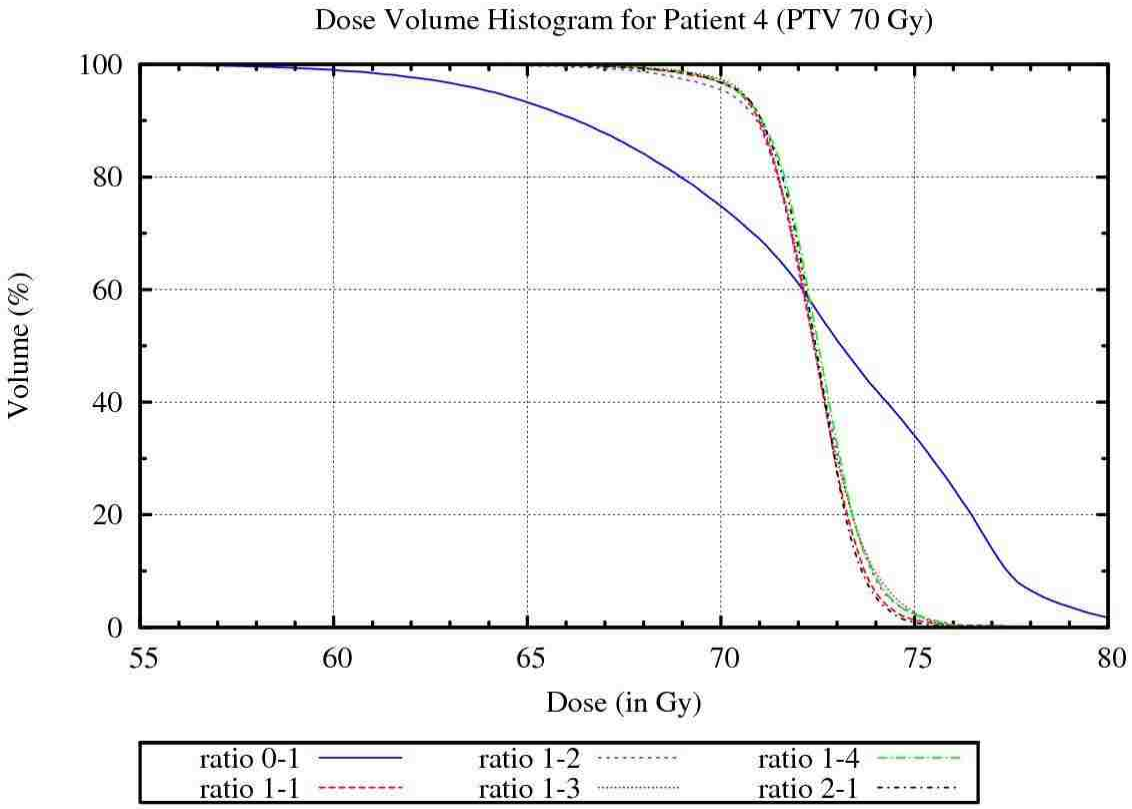

Figure 30 DVH for patient 4 for the PTV of the mixed beam plans

For the OARs displayed in Figure 31, the 0:1 ratio (electron only) plan gave the lowest maximum and mean doses to the OARs. The 1:3 and 1:4 ratio plan show a smaller volume receiving both high and low doses for the left lens and left eye than the other mixed beam plans. The 2:1 ratio plan gives a smaller volume to high doses for the left optic nerve than the other mixed beam plans, however, all the plans gave clinically acceptable maximum dose for the optic nerves.

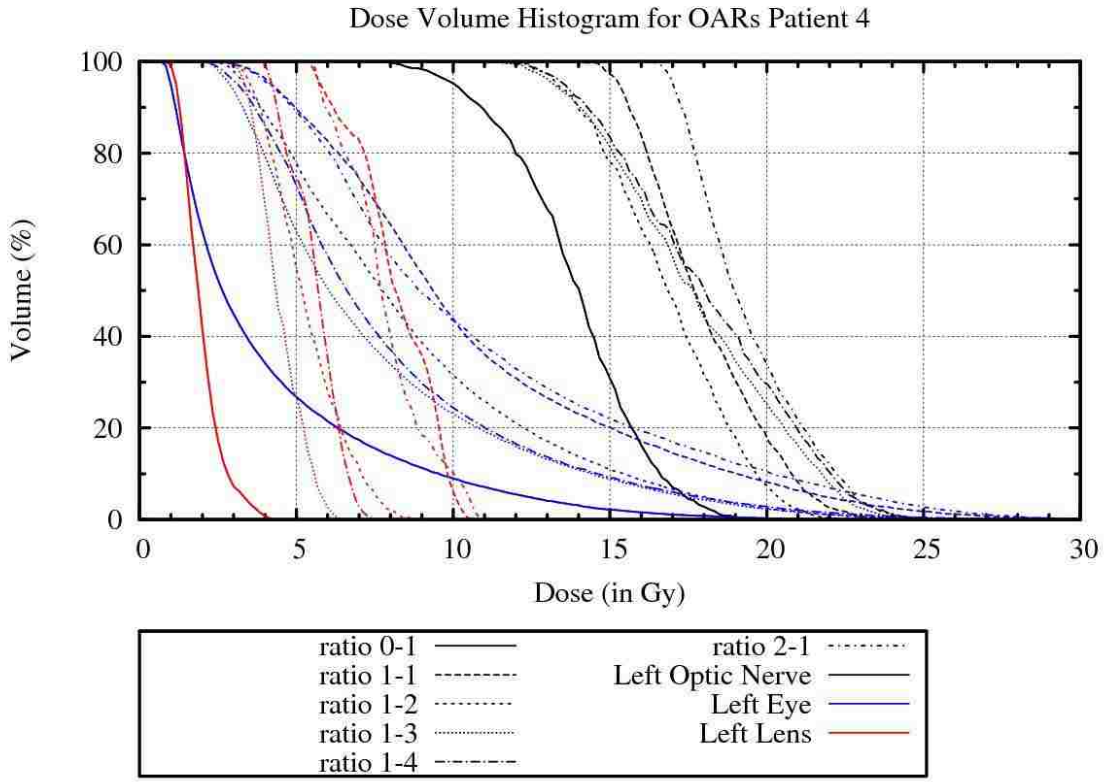

Figure 31 DVH for patient 4 for the OARs of the mixed beam plans

3.5.3.2 Select mixed beam, HT, and IMRT

DVHs for the PTV and OARs for the HT, IMRT, and selected mixed beam (1:3 ratio) are shown in Figure 32. The HT plan showed a lower volume of dose receiving over the prescription dose than the IMRT or mixed beam plan while having a similar minimum dose. The mixed beam plan gave the lowest maximum left eye and left lens dose.

3.5.4 Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of the HT, IMRT, and the mixed beam plans and found the plans to be marginally acceptable. A complete list of individual plan reviews can be found in Appendix A.

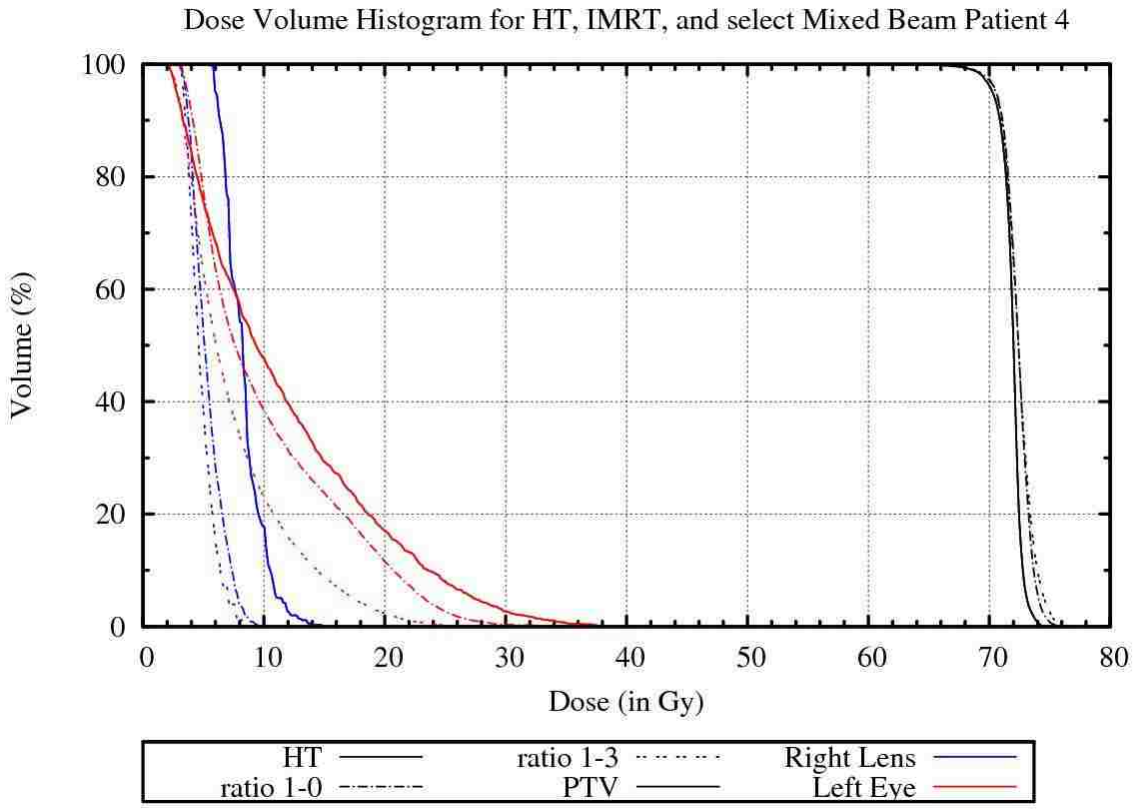

Figure 32 DVH for patient 4 for the PTV and OARs for the HT, IMRT, and select mixed beam plans

After reviewing the dose distributions and DVHs for all the plans, he was indifferent on how the HT plan compared to the mixed beam plan. No comment was provided on his decision. The radiation oncologist did suggest that if nodal involvement had occurred, treating with the mixed beam fields would become more complicated and he disliked having to treat patients with multiple modalities.

3.5.5 Dose Statistics for the PTV and TCP

3.5.5.1 All mixed beam plans

Table 21 gives the dose statistics for the PTV for the mixed beam plans. The high TCP values were recorded in all plans, statistically 100%. Conformity index (CI) was highest for the 1:1 ratio plan (0.852). CI trended down passed the 1:1 ratio. DHI was largest for the electron only plan at 0.290 which was improved to 0.089 by the addition of electrons in the 2:1 ratio plan. This was only a slight from the IMRT only plan's conformity of 0.086.

Table 21 Dose statistics for the PTV for the mixed beam plans for patient 4

PTV – Patient 4					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
1:0	100.0	0.755	0.086	74.7	68.7
2:1	100.0	0.842	0.089	74.8	68.6
1:1	100.0	0.852	0.095	75.1	68.5
1:2	100.0	0.846	0.113	75.6	67.7
1:3	100.0	0.826	0.093	75.4	68.9
1:4	100.0	0.824	0.097	75.5	68.7
0:1	99.9	0.746	0.290	80.5	60.2

Table 22 Dose statistics for the PTV for the HT, IMRT, and select mixed beam plan for patient 4

PTV – Patient 4					
Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
HT	100.0	0.798	0.074	73.9	68.7
1:0	100.00	0.755	0.086	74.7	68.7
1:3	100.0	0.826	0.093	75.4	68.9

3.5.5.2 Select mixed beam, HT, and IMRT plans

Table 22 gives the dose statistics for the PTV for the HT, IMRT and select mixed beam plan. Similar to the mixed beam plans, the patient had high TCP values for all three cases. This is most likely due to the higher dose required to control the infiltrating moderately differentiated cancer. CI was highest for the 1:3 ratio plan (0.826) but closely followed by the HT plan (0.798). DHI was the best for the HT (0.074) and degraded to 0.093 for mixed beam.

3.5.6 Dose Statistics of the OARs and NTCPs

Table 23 and Table 24 display the related dose statistics for the OARs and NTCPs for patient 4.

3.5.6.1 Lens

3.5.6.1.1 All mixed beam plans

Table 23 Dose statistics for the OARs for the mixed beam plans for patient 4

Critical Structures – Patient 4										
	Left lens		Right lens		Left eye		Right eye		Right optic nerve	Left optic nerve
Plan	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	Dmax
1:0	8.9	0.6	9.9	0.6	36.0	<0.1	39.2	<0.1	36.6	32.7
2:1	11.0	2.2	9.6	0.8	32.1	<0.1	33.2	<0.1	30.1	25.1
1:1	10.6	2.6	9.8	0.9	32.3	<0.1	33.8	<0.1	30.0	24.0
1:2	8.8	0.6	8.0	0.4	27.5	<0.1	32.3	<0.1	27.7	22.5
1:3	6.6	0.3	8.5	0.4	28.4	<0.1	33.5	<0.1	27.8	25.0
1:4	7.6	0.6	9.2	0.5	30.2	<0.1	33.0	<0.1	26.8	25.4
0:1	4.3	0.1	7.8	0.2	22.7	<0.1	30.0	<0.1	23.0	19.5

Maximum dose and NTCP for cataract requiring (surgical) intervention was computed for the lens. The electron only had both the lowest left and right lens maximum dose (4.3 Gy and 7.8 Gy respectively) along with the lowest NTCP value (0.1 and 0.2 respectively). The maximum doses for the lens for the IMRT plan was reduced (8.9 Gy and 9.9 Gy, respectively) to (6.6 Gy and 8.5 Gy) by the 1:3 ratio mixed beam plan.

3.5.6.1.2 Select mixed beam (1:3), HT, and IMRT plan

The mixed beam plan gave a lower maximum dose to the lens than the HT or IMRT plan did. This corresponded to about a 2% lower NTCP for the right lens than the HT plan, however the left lens was actually slightly lower for the HT plan than the mixed beam plan despite the higher maximum lens dose.

3.5.6.2 Eye and optic nerve

3.5.6.2.1 All mixed beam plans

Maximum dose to the eyes was highest for the HT plan (left eye-36 Gy and right eye-39.2 Gy) and also for the optic nerve (however the dose was clinically acceptable). The lowest dose for the eyes and optic nerve was the electron only plan. Incorporating the IMRT into the electron only plan for the optic eyes raised the maximum dose from 22.7 Gy and 30.0 Gy to 28.4 Gy and 33.5 Gy, respectively (compared to IMRT 36.0 Gy and 39.2 Gy).

3.5.6.2.2 Select mixed beam, HT, and IMRT plan

Maximum dose was computed for both the eyes and optic nerves, along with the NTCP for blindness for the lens. Similar to the results with the lens, the mixed beam plan saw a significant decrease in maximum eye dose compared to the HT or the IMRT plan. The risk for complication was low in all

three plans. Again the mixed beam plan resulted in a lower maximum dose for the optic nerve than the IMRT or HT plan.

Table 24 Dose statistics for the OARs for the HT, IMRT, and select mixed beam plan for patient 4

Critical Structures – Patient 4										
	Left lens		Right lens		Left eye		Right eye		Right optic nerve	Left optic nerve
Plan	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	Dmax
HT	8.0	0.3	14.9	2.8	40.5	<0.1	37.6	<0.1	30.6	33.4
1:0	8.9	0.6	9.9	0.6	36.0	<0.1	39.2	<0.1	36.6	32.7
1:3	6.6	0.3	8.5	0.4	28.4	<0.1	33.5	<0.1	27.8	25.0

3.5.7 Non-specific Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 1863 cm^3 for the HT plan, 1256 cm^3 for the IMRT plan, and 728 cm^3 for the mixed beam plan. The difference in volume between the HT and the mixed beam plan was 1135 cm^3. Normalizing the volumes to the HT plan, the mixed beam plan gave 39% volume.

3.6 Patient Five – Nasal Cavity

3.6.1 Patient Specific Information

A 90 year old female was diagnosed to have squamous cell carcinoma of the left nasal septum, cT1N0M0. She underwent primary radiotherapy for her nasal cancer at a dose of 63 Gy in 28 fractions using a mix of 6 MV photons and 12 MeV electrons while the patient had a Cerrobend mask with custom bolus nose plugs.

3.6.2 Isodose Distributions

Isodose distributions for HT, IMRT (1:0), and a selected mixed beam plan (1:4 ratio) are displayed in Figure 33-35. Dose statistics for the isodose distributions can be found in Table 26 for the PTV and Table 28 for the critical structures. The white lines in the CT images indicate the position of the orthogonal planes and the red colorwash indicates the primary PTV. The red isodose line represents the desired prescription dose (65.0 Gy) to the PTV.

3.6.2.1 HT

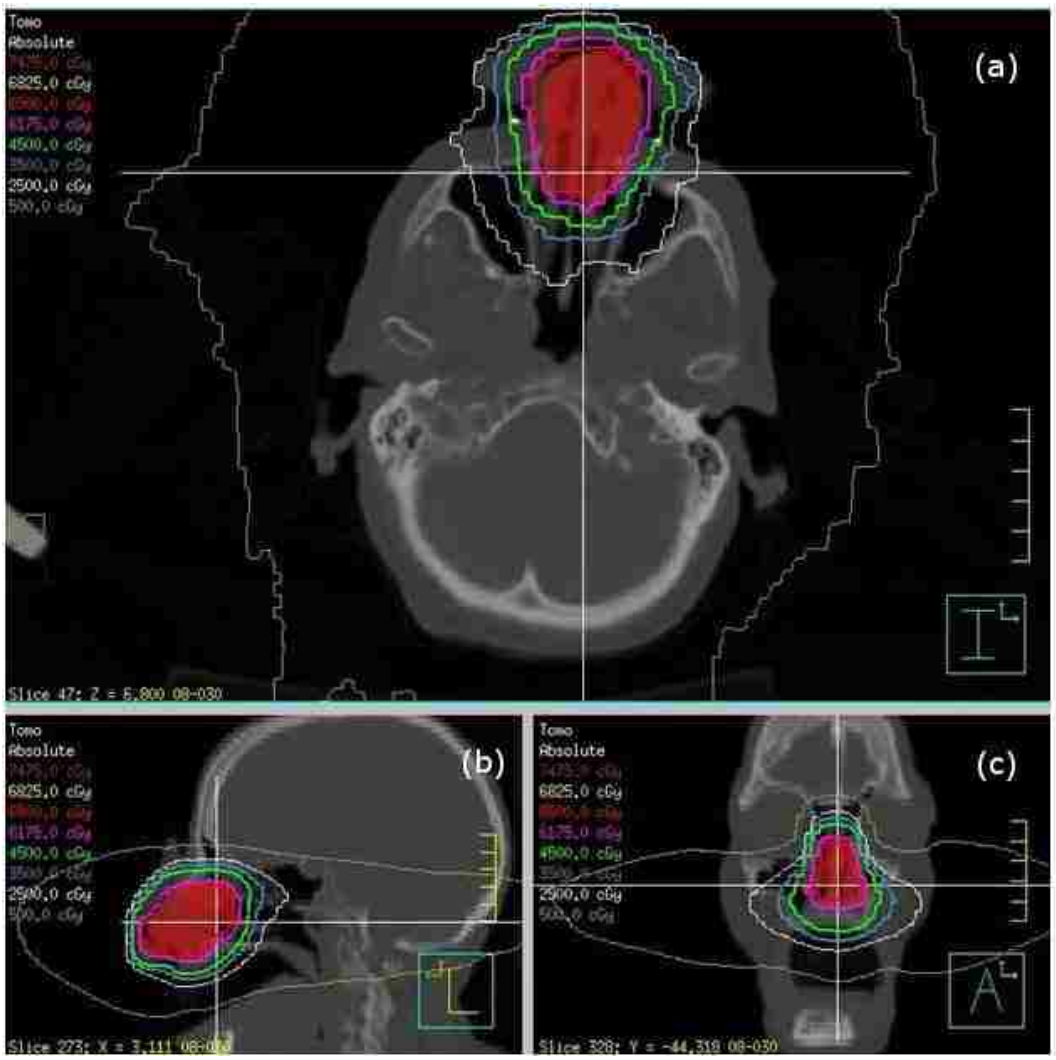

Figure 33 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 5 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The HT isodose distribution showed more conformal coverage than the IMRT and mixed beam plans. No hot or cold spots greater than 5% were observed in the PTV for the HT plan. The HT plan showed a steep lateral dose fall off to 35 Gy from the PTV compared to the IMRT only plan.

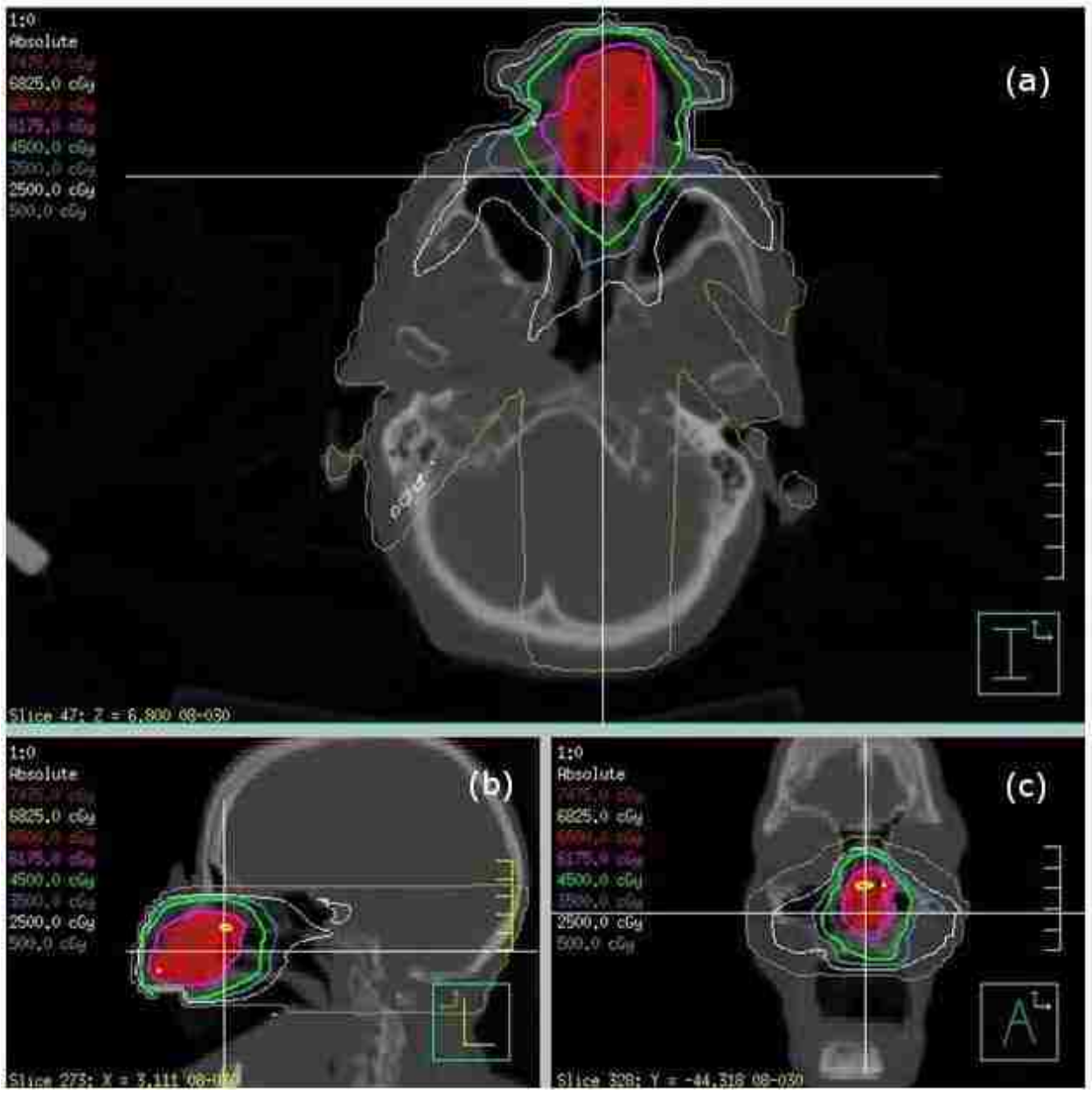

Figure 34 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 5 for the IMRT (1:0) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The HT plan showed a steep distal dose fall off to 45 Gy from the PTV compared to the mixed beam plan. The HT plan showed a larger area of tissue outside the PTV receiving a dose greater than 5 Gy than compared to the mixed beam plan.

3.6.2.2 IMRT/Mixed Beam

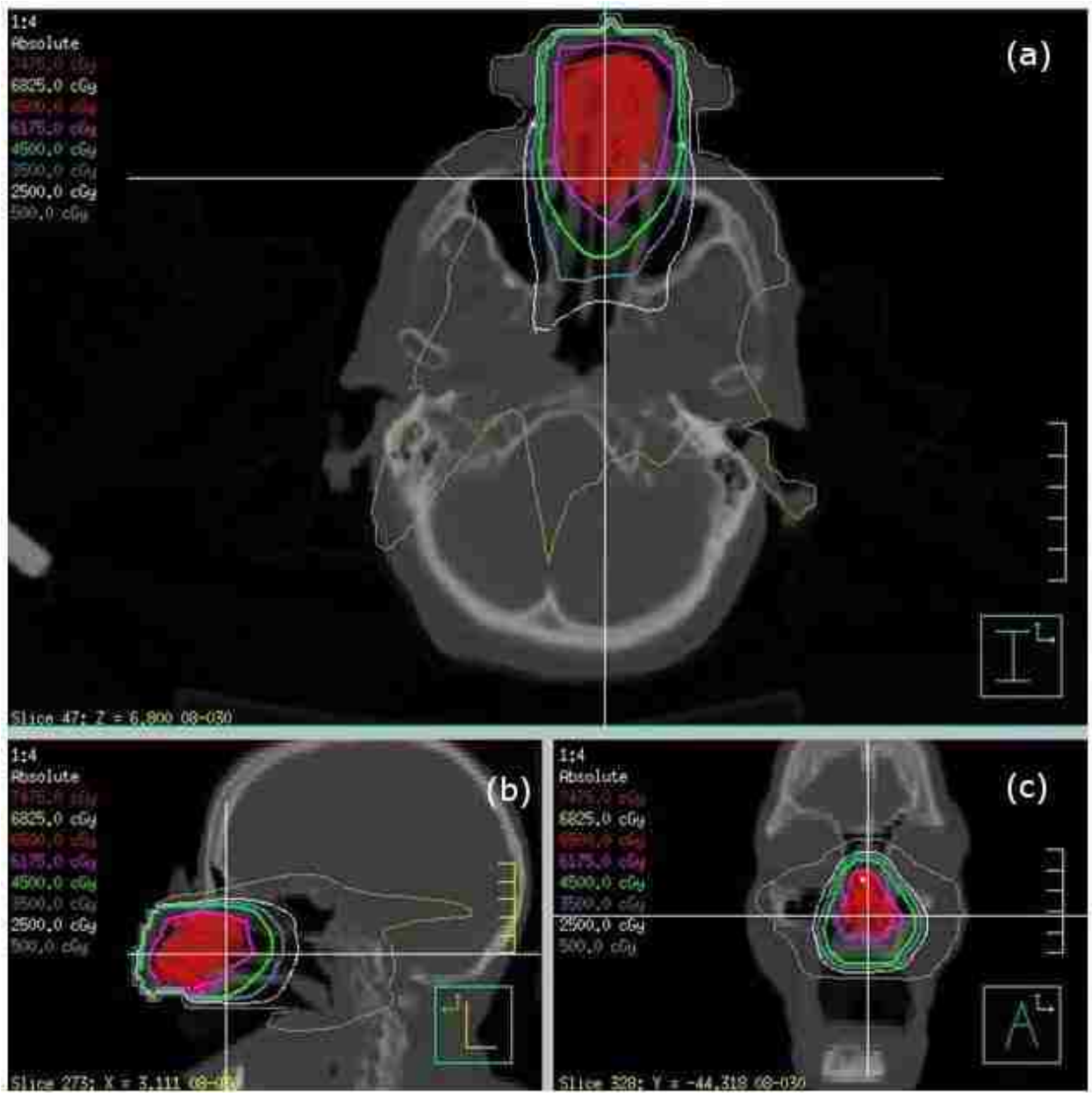

Figure 35 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV for patient 5 for the IMRT + electron (1:4) plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as in red colorwash.

The IMRT and selected mixed beam isodose distributions showed light 5% hot and cold spots. In the IMRT plan, the distal edge of the PTV has the 5% cold spot, purple isodose line (61.75 Gy), breaches the PTV. For the mixed beam plan, there is a 5% cold spot near the orbit of the left eye. Both the IMRT and mixed beam plan show a small hot spot near the superior-posterior region of the PTV. The IMRT and mixed beam plan isodose distributions exhibited similar fall off distal to the PTV, but the mixed beam plan showed a sharper fall lateral to the beam's edge.

3.6.3 DVH Comparisons

3.6.3.1 All mixed beam plans

DVH comparisons for the PTV and OARs for the mixed beam plans are shown in Figure 36 and Figure 37, respectively.

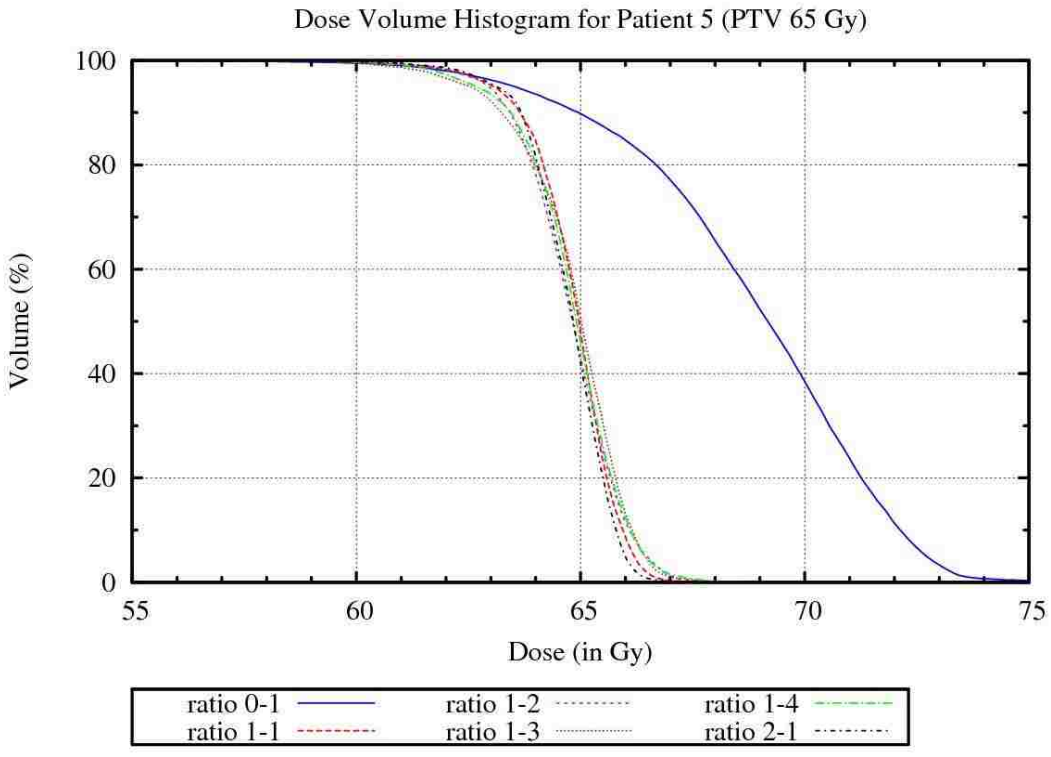

Figure 36 DVH for patient 5 for the PTV of the mixed beam plans

The mixed beam plans all showed similar PTV dose volume coverage with the exception of the 0:1 ratio (electron only) plan, which was significantly less conformal and had a higher maximum dose to the PTV.

For the OARs, the 0:1 ratio plan gave the lowest mean and max dose eyes and lens, followed by the 1:4 and 2:1 ratio mixed beam plan. There did not appear to be a strong correlation between the electron involvement maximum doses for the mixed beam plan.

3.6.3.2 Select mixed beam, HT, and IMRT

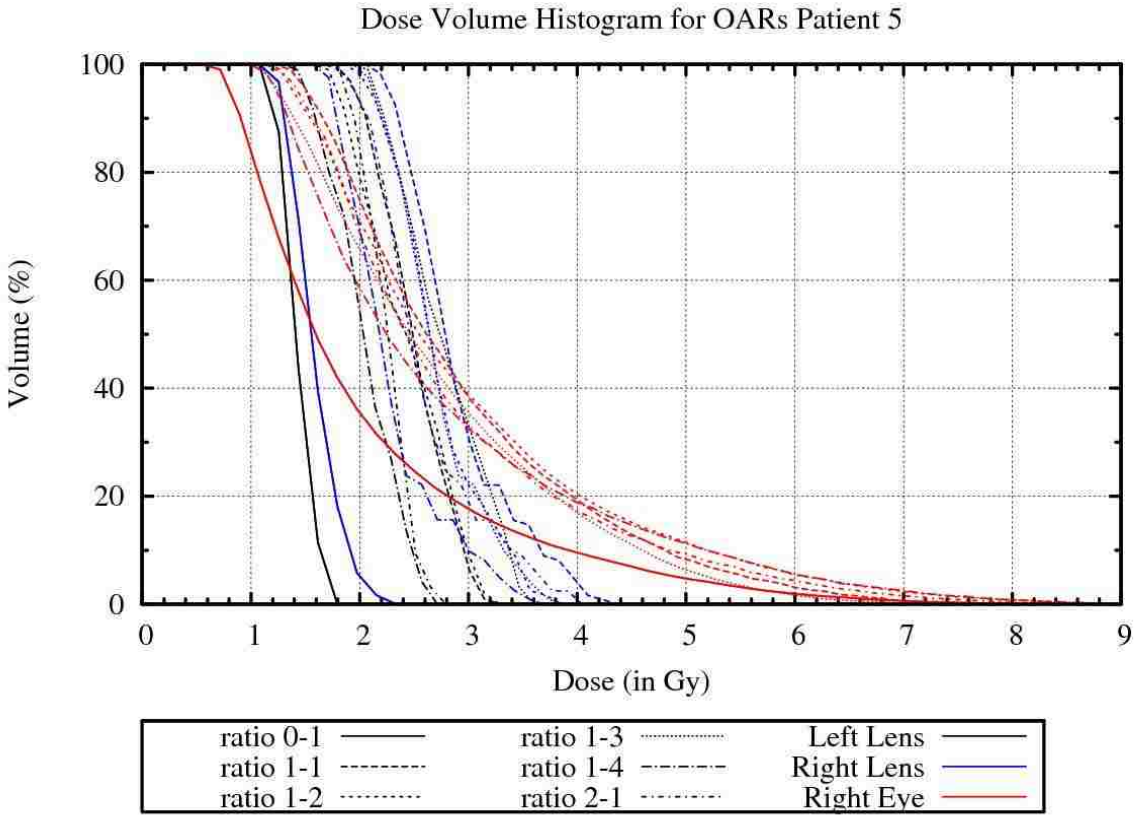

Figure 37 DVH for patient 5 for the OARs of the mixed beam plans

DVHs for the PTV and OARs for the HT, IMRT, and selected mixed beam (1:4 ratio) are shown in Figure 38. The HT plan showed a smaller volume of the PTV receiving greater than and less the prescription dose of 65 Gy compared to the IMRT and mixed beam plan. It should be noted that the

mixed beam plan appears to give a more uniform dose than the IMRT plan, however less uniform than the HT plan.

For the OARs, the lens dose among the plans was similar. The left eye shows a higher yet still clinically acceptable maximum dose for the IMRT plan. The HT plan gives a lower maximum dose to the left eye than the select mixed beam plan.

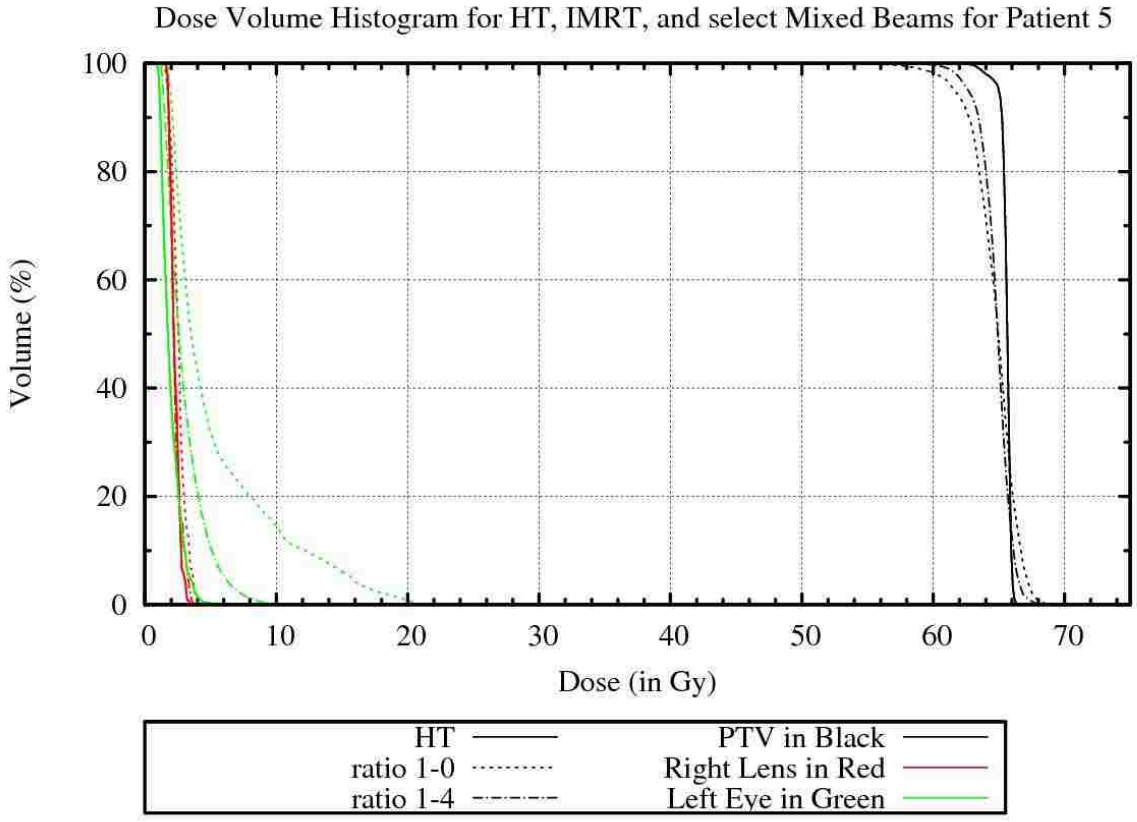

Figure 38 DVH for patient 5 for the PTV and OARs for the HT, IMRT, select mixed beam plans

3.6.4 Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of the HT, IMRT, and mixed beam plans and found the HT plan to be marginally acceptable, indifferent about the IMRT plan, and found the best mixed beam ratio to be acceptable. A complete list of individual plan reviews can be found in Appendix A. After reviewing the dose distributions and DVHs for all the plans, he ranked the

TomoTherapy plan marginally inferior to the mixed beam plan. Being able to shield the eye was listed as a reason for preferring mixed beam plan over the HT plan. The radiation oncologist suggested that he felt more confident treating around the lens with lead shielding in place.

3.6.5 Dose Statistics for the PTV and TCP

3.6.5.1 All mixed beam plans

Table 25 gives the dose statistics for the PTV for the mixed beam plans. The TCP values were comparable (within ± 0.1% of 100.0% tumor control) for all the plans. Conformity index (CI) was highest for the 0:1 ratio plan (0.573) followed closely by the 1:3 plan with 0.436. Dose homogeneity index varied among the plan and was best for the 2:1 ratio plan (DHI=0.071) and ranged to the worst value of 0.191 for the 0:1 ratio plan.

Table 25 Dose statistics for the PTV for the mixed beam plans for patient 5

PTV – Patient 5						
Patient 5	Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
	1:0	100.0	0.413	0.138	67.9	58.9
	2:1	100.0	0.333	0.071	66.3	61.7
	1:1	100.0	0.397	0.078	66.6	61.5
	1:2	100.0	0.374	0.083	67.0	61.5
	1:3	100.0	0.436	0.096	67.0	60.7
	1:4	100.0	0.404	0.090	67.1	61.3
	0:1	100.0	0.573	0.191	73.6	61.2

3.6.5.2 Select mixed beam (1:4), HT, and IMRT plans

Table 26 gives the dose statistics for the PTV from the HT, IMRT, and select mixed beam plans. The TCP values were within ± 0.1% of 100.0% tumor control.

Table 26 Dose statistics for the PTV for the HT, IMRT, and select mixed beam plan for patient 5

PTV – Patient 5						
Patient 5	Plan	TCP (%)	CI	DHI	Dmax (Gy)	Dmin (Gy)
	HT	100.0	0.797	0.039	66.1	63.5
	1:0	100.0	0.413	0.138	67.9	58.9
	1:4	100.0	0.404	0.090	67.1	61.3

The CI for the IMRT plan and the mixed beam plan were similar (IMRT=0.413 and 1:4 ratio=0.404). The HT plan however had a much higher CI of 0.797. The HT plan showed a lower DHI value than the mixed beam or the IMRT plan, indicating the HT plan was more homogeneous over the PTV.

3.6.6 Dose Statistics of the OARs and NTCPs

3.6.6.1 Lens and Eyes

3.6.6.1.1 All mixed beam plans

Table 27 gives the dose statistics for the lens and eyes for the mixed beam plans. Maximum dose was calculated, along with the NTCP of cataract requiring (surgical) intervention for the lens and NTCP of blindness for the eyes.

Table 27 Dose statistics for the OARs for the mixed beam plans for patient 5

Critical Structures – Patient 5									
		Left lens		Right lens		Left eye		Right eye	
patient 5	Plan	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)
	1:0	3.5	0.1	4.0	0.1	22.0	<0.1	9.1	<0.1
	2:1	2.8	0.1	4.0	0.1	12.3	<0.1	9.1	<0.1
	1:1	3.3	0.1	4.4	0.1	12.7	<0.1	8.7	<0.1
	1:2	3.3	0.1	3.9	0.1	12.0	<0.1	10.1	<0.1
	1:3	3.6	0.1	3.9	0.1	10.1	<0.1	7.8	<0.1
	1:4	2.7	0.1	3.7	0.1	10.6	<0.1	9.7	<0.1
	0:1	1.8	<0.1	2.3	<0.1	17.1	<0.1	8.4	<0.1

As seen in the DVHs, the 1:4 and 0:1 gave the lowest maximum dose to the lens (2.7 Gy and 1.8 Gy for the left lens and 3.7 Gy and 2.3 Gy for the right lens, respectively). Compared to the IMRT plan at 3.5 Gy for the left and 4.0 Gy for the right, the mixed beam plan slightly reduced the lens dose. NTCP were overall low for both the lens and eyes for both plans (below 0.1%).

3.6.6.1.2 Select mixed beam plan, HT, and IMRT plan

Table 28 gives the dose statistics for the lens and eyes for the HT, IMRT, and select mixed beam plans. Maximum dose was calculated, along with the NTCP of cataract requiring (surgical) intervention for the lens and NTCP of blindness for the eyes. The mixed beam plan gave the lowest NTCP values for the left and right lens (<0.1and 0.1, respectively) but HT had the lowest maximum right lens dose and a comparable left lens dose to the mixed beam plan. The IMRT plan had a higher maximum dose for both the lens and left eye. Overall, the HT plan was able to provide a plan with the best DHI while giving low dose to the OARs.

Table 28 Dose statistics for the OARs for the HT, IMRT, and select mixed beam plan for patient 5

Critical Structures – Patient 5									
		Left lens		Right lens		Left eye		Right eye	
patient 5	Plan	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)	Dmax	NTCP(%)
	HT	2.9	0.1	3.5	0.1	6.4	<0.1	8.6	<0.1
	1:0	3.5	0.1	4.0	0.1	22.0	<0.1	9.1	<0.1
	1:4	2.7	<0.1	3.7	0.1	10.6	<0.1	9.7	<0.1

3.6.7 Non-specific Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 1152 cm^3 for the HT plan, 721 cm^3 for the IMRT plan, and 515cm^3 for the mixed beam plan. The difference in volume

between the HT and the mixed beam plan was 627 cm^3. Normalizing the volumes to the HT plan, the mixed beam plan gave 45% volume.

3.7 Summary: Tables of Review

Table 29 shows the summary of the radiation oncologist review of the treatment plans for HT and mixed beam.

Table 29 Summary of the radiation oncologist plan review

Patient	Plan acceptable?		Preferred modality	Reason for choice of HT or Mixed Beam
	HT	Mixed Beam		
1	Acceptable	Marginally acceptable	HT	Better PTV coverage and less dose to critical structure near the PTV for HT
2	Acceptable	Acceptable	Indifferent	HT better PTV coverage but more dose to distal critical structures
3	Marginally acceptable	Indifferent	HT	Significant improvement in dose uniformity in PTV for HT
4	Marginally acceptable	Marginally acceptable	Indifferent	Disliked the use of more than one modality (treating nodal spread) in mixed beam
5	Marginally acceptable	Acceptable	Mixed Beam	Preferred the ability to shield the eyes for mixed beam

The HT plans were generally found to be better because of coverage and improvements in dose uniformity in the PTV as seen in patient 1 and 3.

The mixed beam plans were generally found to be comparable or better to HT plans because of distal organ sparing (e.g. contralateral parotid) and that the physician trusted and preferred the eye shielding.

Table 30 shows a summary of the dose homogeneity index for the HT and mixed plan beam plan and the difference between them.

Table 30 Summary of the dose homogeneity index for the HT and mixed beam plan

DHI summary			
	Modality	DHI	DHI difference
Patient 1	HT	0.063	
	Mixed Beam	0.089	0.026
Patient 2	HT	0.017	
	Mixed Beam	0.054	0.037
Patient 3	HT	0.081	
	Mixed Beam	0.186	0.105
Patient 4	HT	0.074	
	Mixed Beam	0.093	0.019
Patient 5	HT	0.039	
	Mixed Beam	0.090	0.051

The DHI was lower for HT in all five patients. The largest difference between the DHIs occurred for patient 3 and the smallest difference for patient 4.

Table 31 Summary of the normal tissue volumes receiving between 25 Gy and 5 Gy

Volume between 25 Gy and 5 Gy isodose			
	Modality	Volume in cc	Normalized to HT
Patient 1	HT	1129	100%
	Mixed	1182	104%
Patient 2	HT	4051	100%
	Mixed	1235	31%
Patient 3	HT	3003	100%
	Mixed	2639	87%
Patient 4	HT	1863	100%
	Mixed	728	39%
Patient 5	HT	1152	100%
	Mixed	515	45%

Table 31 shows a summary of the volume of normal tissue receiving between 25 Gy and 5 Gy. Volumes are shown in cc and then normalized to HT's volume. For all but patient 1, the HT plan irradiates more normal tissue to the dose levels.

Chapter 4 Discussion

This study compared helical tomotherapy to mixed beam (IMRT and electrons) for parotid gland and nasal cavity tumors. Dosimetric and biological metrics were calculated and used to evaluate the plans, in addition to a clinical evaluation based on a radiation oncologist's review.

The results of this research do not support the hypothesis that HT plans have improved dose homogeneity with equal or better normal tissue sparing than mixed beam treatments for select superficial head and neck cancers. Our results showed that HT plan did provide better dose homogeneity than the mixed beam plans. In all five patients, the DHI of HT was better than that in the mixed beam plans, with the largest differences observed in patients 3 and 5. However, HT plans did not have equal or better normal tissue sparing than the mixed beam treatments for all the organs of interest. For example, the contralateral parotid received a lower mean dose in all patients from the mixed beam plan, which resulted in a lower NTCP value for salivary flow reduction. For patients 1, 2, 3, and 4, the eyes and the lens received a lower maximum dose with the mixed beam plan than with the HT plan. However, the HT delivered a lower maximum dose to the spinal cord and lower volume of high dose to the brain than mixed beam, as seen in patient 3.

Three specific aims were completed to test the hypothesis. In Aim 1, five patients were selected that had superficial PTVs (limited to a 5.5 cm depth), among these were 3 parotid tumors and 2 nasal cavity tumors.

In Aim 2, these patients were planned using both the TomoTherapy Hi-Art (for the HT plans) and Pinnacle treatment system (for the mixed beam plans). Planning parameters (pitch, jaw width, etc) and optimization of the HT plan followed typical clinical protocol for head and neck plans. For the mixed beam plans, seven different ratios of photons to electrons were investigated and optimization procedure for the mixed beam plans was as follows. For each trial, the electron ratio for the prescribed dose was delivered by a single electron beam to a point in the PTV. Following the dose computation for the

electron beam, Pinnacle's inverse-planning method was used by the IMRT photons to contribute dose to deficient volumes in the PTV.

In Aim 3, a clinical, dosimetric, and biological evaluation was made of the plans.

4.1 Outcome of Clinical Comparison

The clinical evaluation consisted of a radiation oncologist review of the plans for clinical acceptability and to determine how the HT plan compared to the mixed beam plan. After reviewing the spatial dose distributions and superimposed DVHs of both the HT and mixed beam plans, the radiation oncologist ranked the HT plan to be superior and marginally superior for parotid patients 1 and 3 and was indifferent about the HT plan for parotid patient 2 when compared to the mixed beam plans. The radiation oncologist ranked the HT plan to be indifferent for nasal cavity patient 4 and marginally inferior for nasal cavity patient 5 when compared to the mixed beam plans.

The basis for his judgment was his clinical experience. Some of the reasons he chose the HT plan over the mixed beam were 1) Improved PTV uniformity and coverage, 2) the ability of HT plans to spare specified OARs in close proximity to the PTV, 3) the ability to treat, if desired, separate nodal involvement, without have to match abutting fields, and 4) the absence of having to use more than one modality to treat. On the other hand, he had concerns about lens and eye dose in the nasal cavity patients and preferred to have shielding for the eyes.

4.2 Outcome of Dosimetric Comparison

The dosimetric evaluation consisted of computing the maximum and minimum doses in the PTV, CI of the PTV, DHI within the PTV and also mean and maximum doses for OARs. The results of the dosimetric evaluation showed that HT plans had lower DHI values in all plans and in general trended to have higher CI values than the mixed beam plans. The mean dose to the contralateral parotid was higher for the HT plans.

4.3 Outcome of Biological Comparison

The biological evaluation consisted of computing TCP, NTCP, and volumes of normal tissue irradiated to low dose. The results showed similar TCP values for the HT and mixed beam plans. Slightly higher NTCP values for the lens and also for distal organs such as the contralateral parotid. For all but patient 1, the volume of normal tissue irradiated to a dose between 5 Gy and 25 Gy (dose likely to induce secondary cancers, Schneider *et al*. 2005) was larger for the HT plans. While secondary cancers are extremely rare, this may be a concern for younger patients who have longer survival times which may be at risk of radiation induced cancers. However the rarity of this occurring, as suggested by the clinical experience of the radiation oncologist reviewing the plans, may not make it a significant factor when comparing the two plans.

4.4 Connection with Existing Literature

Some of the data from this study are consistent with previous head and neck studies comparing HT to IMRT. For example, Lee *et al*. (2008) found that helical tomotherapy treatment plans were comparable to or slightly better than IMRT plans for treatment of parotid tumors. The comparison of DHI, NTCP, and TCP for HT and IMRT plan of the three parotid patients in this study was consistent with the findings of Lee *et al*. Their average DHI difference between HT and IMRT for the primary PTV was 0.12 compared to this study's average differences of 0.06. NTCP (salivary flow reduction to <25% at 6 wks) for the contralateral parotid was 2.3% for their study and 1.2% in this study. TCP values varied slightly more (8%) in Lee *et al*. study since all patients in that study required multiple PTV targets and only one patient in this study had multiple PTVs.

However, some of our results differ from previous studies that investigated the feasibility of using mixed beams to treat head and neck cancers. For example, Cozzi *et al.*, (2001) found that conventional techniques of mixed photon and electron fields inferior to IMRT treatments in advanced head and neck cancers. Dose homogeneity was significantly worse for the mixed beam plans than the IMRT plans. 4%

of the PTV of their mixed beam plans was outside the 90% isodose while less than 2% of their IMRT plan was. This is inconsistent with this study in that the mixed beam plans had similar PTV coverage and dose homogeneity (as seen in the DVH section of the results). Theses discrepancies may be explained by differences in the optimization of the photon component of the mixed beam. Rather than weighting the two modalities, in this study the IMRT plan was optimized over the electron contribution. Also in this study, we limited patients to more superficial treatment sites. This benefits the electron beam's dose distribution if it falls off before the edge of the PTV.

4.5 Strength of this Study

Because of the optimization of the IMRT plan over the electron beam dose distribution, we were able to compare an advanced mixed beam technique to the HT plans. Another strength of this study was the selection of superficial sites, which made a comparison between mixed beam and IMRT treatments more interesting. The optimization approach and selected sites makes this study unique relative to the existing literature.

4.6 Limitations of this Study

In this study we examined two classes of superficial head and neck cancer, three cases in the parotid gland and two in the nasal cavity, while these sites both met the superficial target criteria; they are quite different in terms of target geometry and adjacent critical structures. In addition, substantial variations in target geometry were noted even within the parotid subset (for example, patient 3 contained three separate PTVs whereas patients 1 and 2 only contained one). As a result, it does not appear that enough sites similar in geometry were chosen to draw definitive conclusions on whether a statistical significance existed between HT and mixed beam plan for these subsets of cancers. However, the variations in treatment sites allowed this work to serve as a preliminary study of the types of superficial sites that would benefit from combinations of electrons and IMRT. Increasing the sample size in both the parotid and nasal cavity patients could help confirm the results of this study.

Another possible limitation could be delivering the mixed beam plans. The IMRT component of the mixed beam plan was used to fill in the areas of the electron dose distribution that did not meet the desired prescription for the PTV. In these regions, potential high dose gradients in the mixed beam plan could introduce hot/cold spots in the presence of slight mismatches in the field alignment. As a result, because multiple modalities were used in the mixed beam plans, additional precautionary measures may be required for ensuring safe delivery.

Finally, it should be noted that the parotid patients were all planned with a bolus to give a high skin dose, especially at surgical scars and to compensate for missing tissue on the surface. In this study the bolus was of uniform thickness. The bolus however could have been a variable thickness bolus compensator in order to improve the dose distribution from the electron beam component. Since the IMRT component fills in the difference between the electron contribution and prescription, the advantage of a variable thickness bolus could reduce large dose gradients utilized in the IMRT plan.

4.7 Future Work

The findings in this study suggest that mixed beam treatments could be used as an effective alternative for reducing the dose to distal critical organs to values near electron beam only while at the same time restoring the TCP to levels near HT and IMRT. The next step is to study how a variable thickness bolus compensator affects the dose distributions. These studies should include the combination of bolus electron conformal therapy with IMRT to improve the DHI values from the mixed beam plans seen in this study. In addition, based on the preliminary results of the different ratios of photons to electrons used in this study, future studies should utilized the heavier electron weighted (1:3 and 1:4 ratios) mixed beam plans and investigate a larger sample of similar patients in order to confirm statistically significance of difference between HT and mixed beam plans.

Chapter 5 Conclusions

The preliminary investigation of HT and mixed beam plans for superficial head and neck cancers showed that HT plans can deliver dose distributions with increased dose conformity and improved dose homogeneity index for three parotid gland and two nasal cavity tumors than mixed beam plans. However, larger volumes of contralateral critical structures (the untreated parotid gland) and normal tissue received low dose with HT in the parotid plans. In the nasal cavity plans, larger volumes of adjacent critical structures (the lens) and normal tissue received low dose with HT. For patients with a single shallow uniform PTV, mixed beam plans yield more favorable PTV and OAR results.

In conclusion, HT plans delivered a more uniform dose distribution to the PTV in all five patients. Based on TCP values and radiation oncologist evaluations, mixed beam plans were also able to deliver clinically acceptable PTV coverage while sparing specified normal tissue (e.g. contralateral parotid gland). However, more studies should be done to address slight variability in the results among the treatment sites and geometries of the PTV.

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Appendix A: Radiation Oncologist Evaluation of Treatment Plans

Radiation Oncologist Evaluation of Treatment Plans
Date:
Patient ID: Patient 1,

a.) Evaluate the clinical acceptability of plans. Please check one category that closely describes your observation for each plan.

Clinical acceptability	Acceptable	Marginally acceptable	Indifferent	Marginally unacceptable	Unacceptable
Photon plans					
TomoTherapy	X				
1:0 IMRT			X		
IMRT with electron plans (photon:electron ratio)					
2:1 IMRT w/electron (ratio in favor of photons)				X	
1:1 IMRT w/ electron				X	
1:2 IMRT w/electron		X			
1:3 IMRT w/electron			X		
1:4 IMRT w/electron			X		
0:1 electrons					X

b.) Compare the TomoTherapy plan with the best IMRT with electron plan.

i. How does the **TomoTherapy** plan compare with the best **IMRT with electron plan**? Please check one category that best describes your observation.

Plan to plan comparison	Superior	Marginally superior	Indifferent	Marginally inferior	Inferior
TomoTherapy vs IMRT w/electrons		X			

Radiation Oncologist Evaluation of Treatment Plans
Date:
Patient ID: Patient 2,

a.) Evaluate the clinical acceptability of plans. Please check one category that closely describes your observation for each plan.

Clinical acceptability	Acceptable	Marginally acceptable	Indifferent	Marginally Unacceptable	Unacceptable
Photon plans					
TomoTherapy	X				
1:0 IMRT	X				
IMRT with electron plans (photon:electron ratio)					
2:1 IMRT w/electron (ratio in favor of photons)	X				
1:1 IMRT w/ electron	X				
1:2 IMRT w/electron	X				
1:3 IMRT w/electron	X				
1:4 IMRT w/electron	X				
0:1 electrons				X	

b.) Compare the TomoTherapy plan with the best IMRT with electron plan.

i. How does the **TomoTherapy** plan compare with the best **IMRT with electron plan**? Please check one category that best describes your observation.

Plan to plan comparison	Superior	Marginally superior	Indifferent	Marginally inferior	Inferior
TomoTherapy vs IMRT w/electrons			X		

Radiation Oncologist Evaluation of Treatment Plans
Date:
Patient ID: Patient 3,

a.) Evaluate the clinical acceptability of plans. Please check one category that closely describes your observation for each plan.

Clinical acceptability	Acceptable	Marginally acceptable	Indifferent	Marginally Unacceptable	Unacceptable
Photon plans					
TomoTherapy		X			
1:0 IMRT			X		
IMRT with electron plans (photon:electron ratio)					
2:1 IMRT w/electron (ratio in favor of photons)				X	
1:1 IMRT w/ electron			X		
1:2 IMRT w/electron				X	
1:3 IMRT w/electron			X		
1:4 IMRT w/electron				X	
0:1 electrons					

b.) Compare the TomoTherapy plan with the best IMRT with electron plan.

i. How does the **TomoTherapy** plan compare with the best **IMRT with electron plan**? Please check one category that best describes your observation.

Plan to plan comparison	Superior	Marginally superior	Indifferent	Marginally inferior	Inferior
TomoTherapy vs IMRT w/electrons	X				

Radiation Oncologist Evaluation of Treatment Plans
Date:
Patient ID: Patient 4,

a.) Evaluate the clinical acceptability of plans. Please check one category that closely describes your observation for each plan.

Clinical acceptability	Acceptable	Marginally acceptable	Indifferent	Marginally Unacceptable	Unacceptable
Photon plans					
TomoTherapy		X			
1:0 IMRT		X			
IMRT with electron plans (photon:electron ratio)					
2:1 IMRT w/electron (ratio in favor of photons)		X			
1:1 IMRT w/ electron		X			
1:2 IMRT w/electron		X			
1:3 IMRT w/electron		X			
1:4 IMRT w/electron		X			
0:1 electrons					X

b.) Compare the TomoTherapy plan with the best IMRT with electron plan.

i. How does the **TomoTherapy** plan compare with the best **IMRT with electron plan**? Please check one category that best describes your observation.

Plan to plan comparison	Superior	Marginally superior	Indifferent	Marginally inferior	Inferior
TomoTherapy vs IMRT w/electrons			X		

Radiation Oncologist Evaluation of Treatment Plans
Date:
Patient ID: Patient 5,

a.) Evaluate the clinical acceptability of plans. Please check one category that closely describes your observation for each plan.

Clinical acceptability	Acceptable	Marginally acceptable	Indifferent	Marginally unacceptable	Unacceptable
Photon plans					
TomoTherapy		X			
1:0 IMRT			X		
IMRT with electron plans (photon:electron ratio)					
2:1 IMRT w/electron (ratio in favor of photons)	X				
1:1 IMRT w/ electron	X				
1:2 IMRT w/electron	X				
1:3 IMRT w/electron	X				
1:4 IMRT w/electron	X				
0:1 electrons			X		

b.) Compare the TomoTherapy plan with the best IMRT with electron plan.

i. How does the **TomoTherapy** plan compare with the best **IMRT with electron plan**? Please check one category that best describes your observation.

Plan to plan comparison	Superior	Marginally superior	Indifferent	Marginally inferior	Inferior
TomoTherapy vs IMRT w/electrons				X	

Appendix B: Isodose Distributions

Patient 1

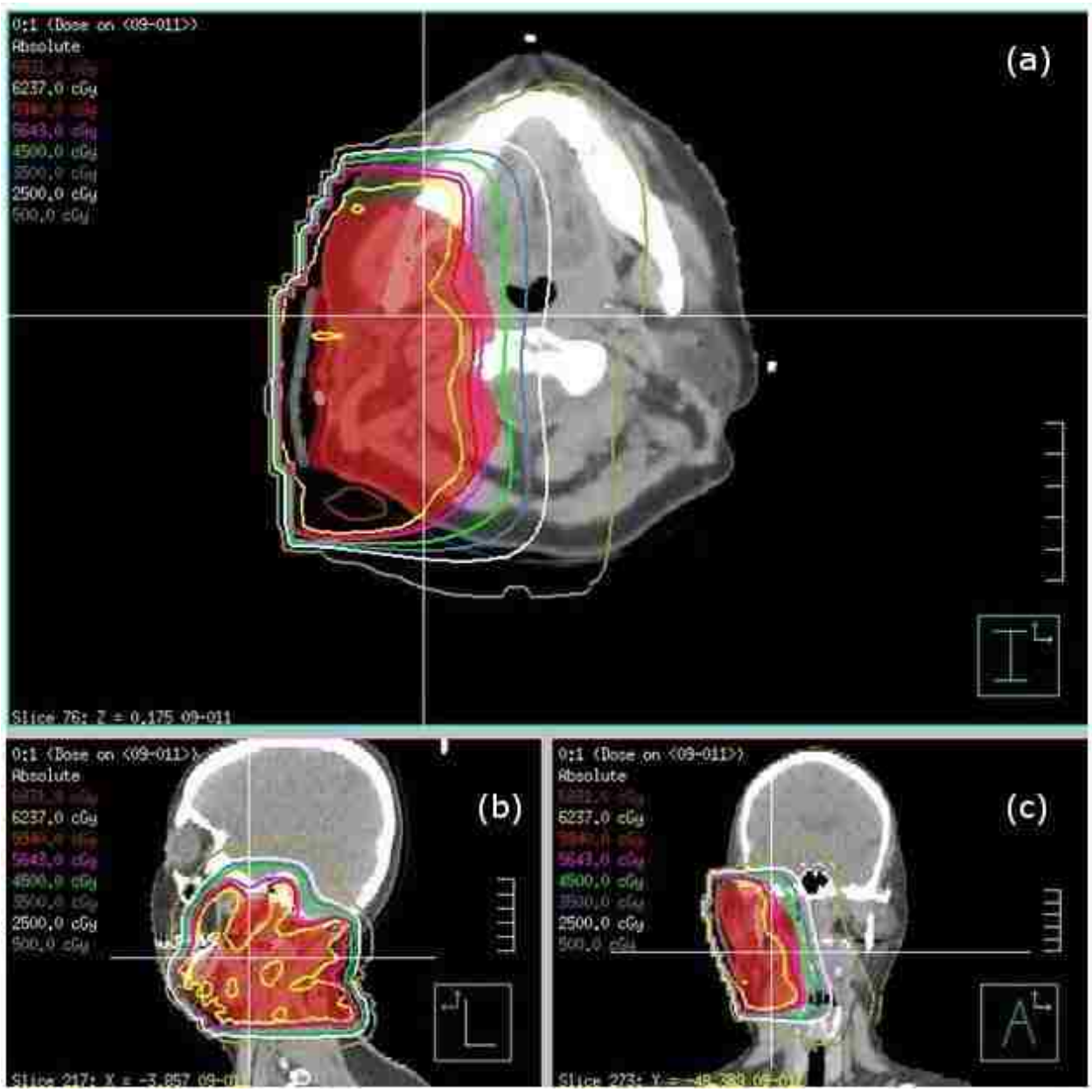

Figure 39 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 0:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

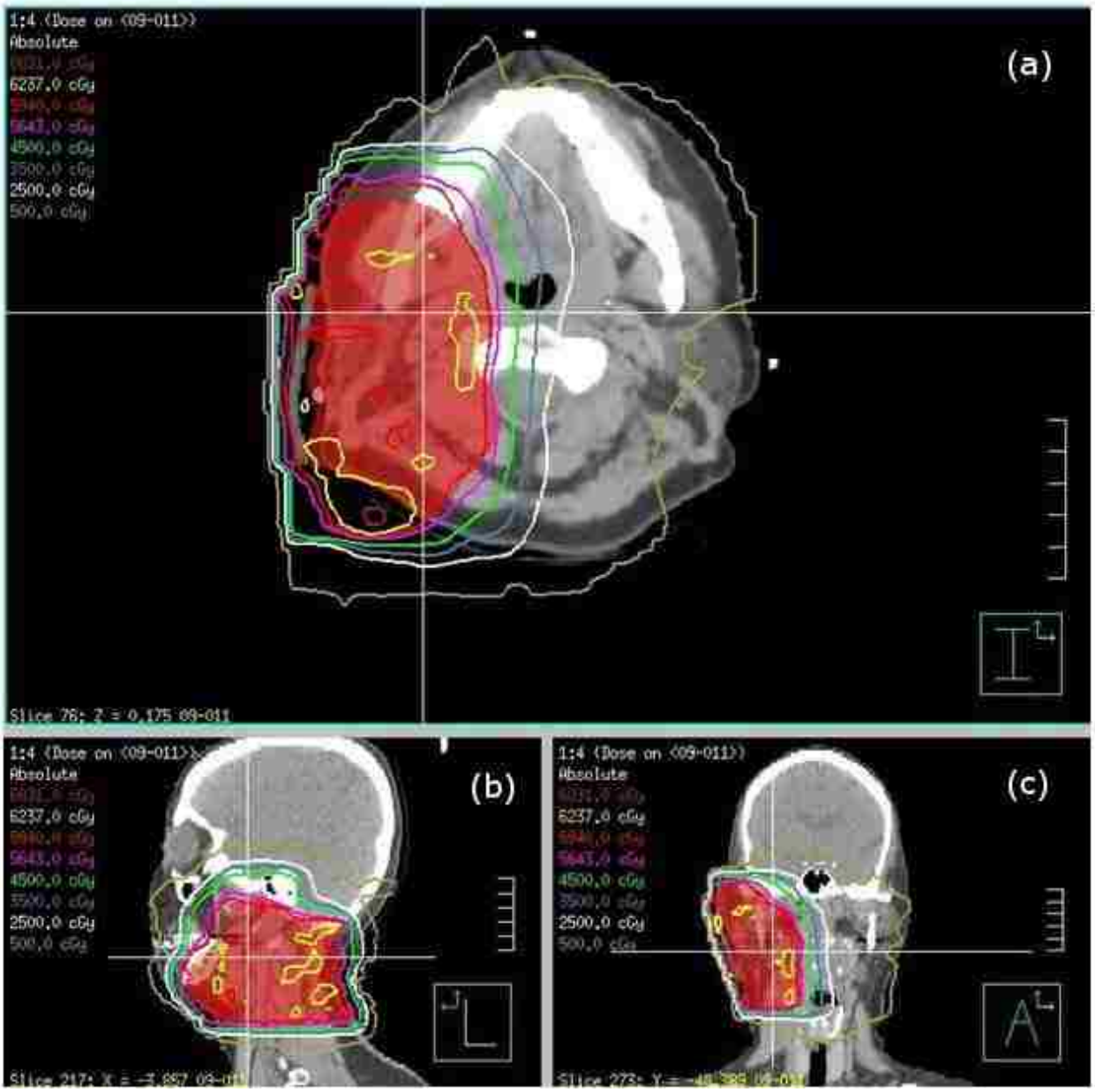

Figure 40 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 1:4 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

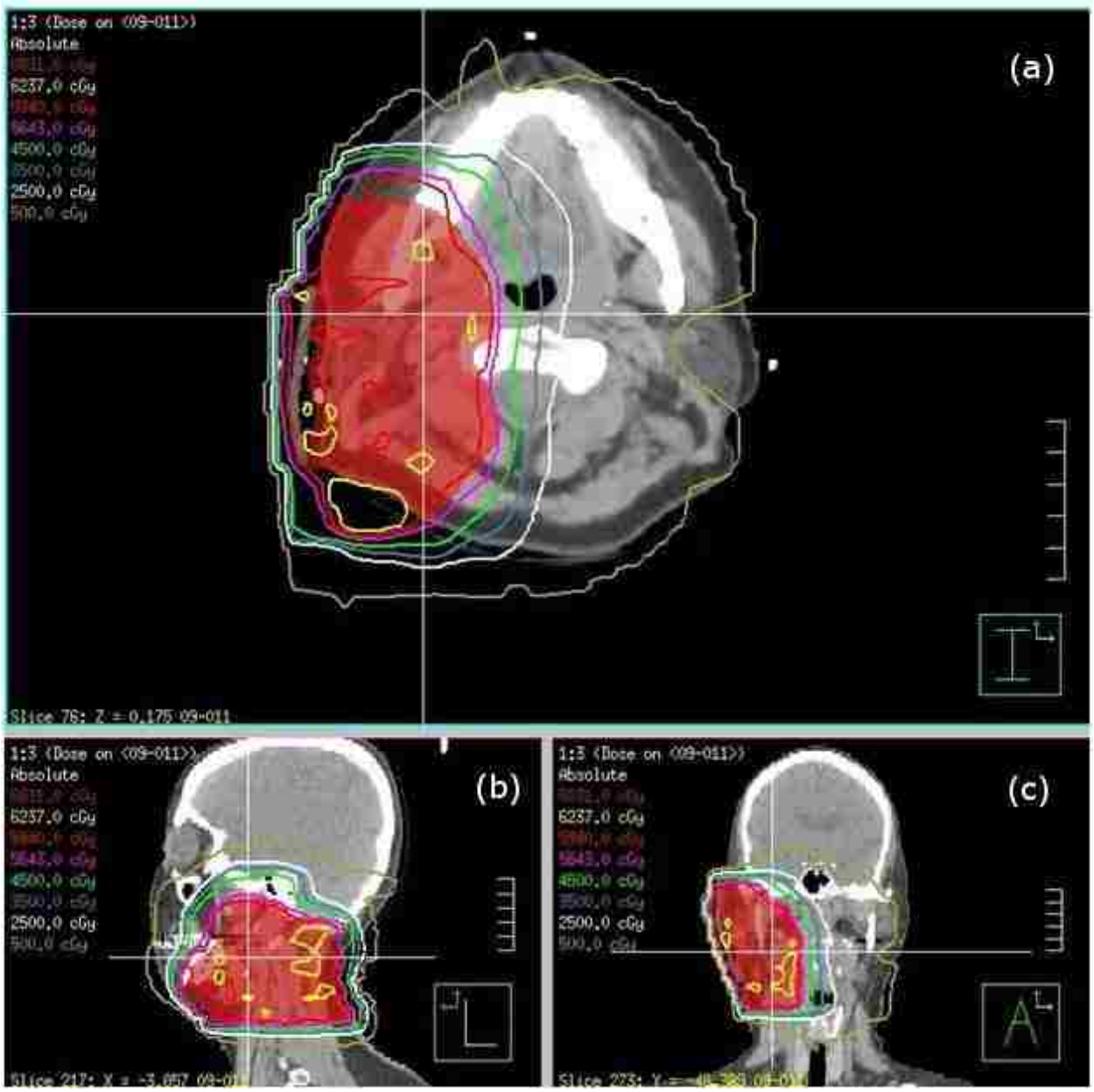

Figure 41 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 1:3 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

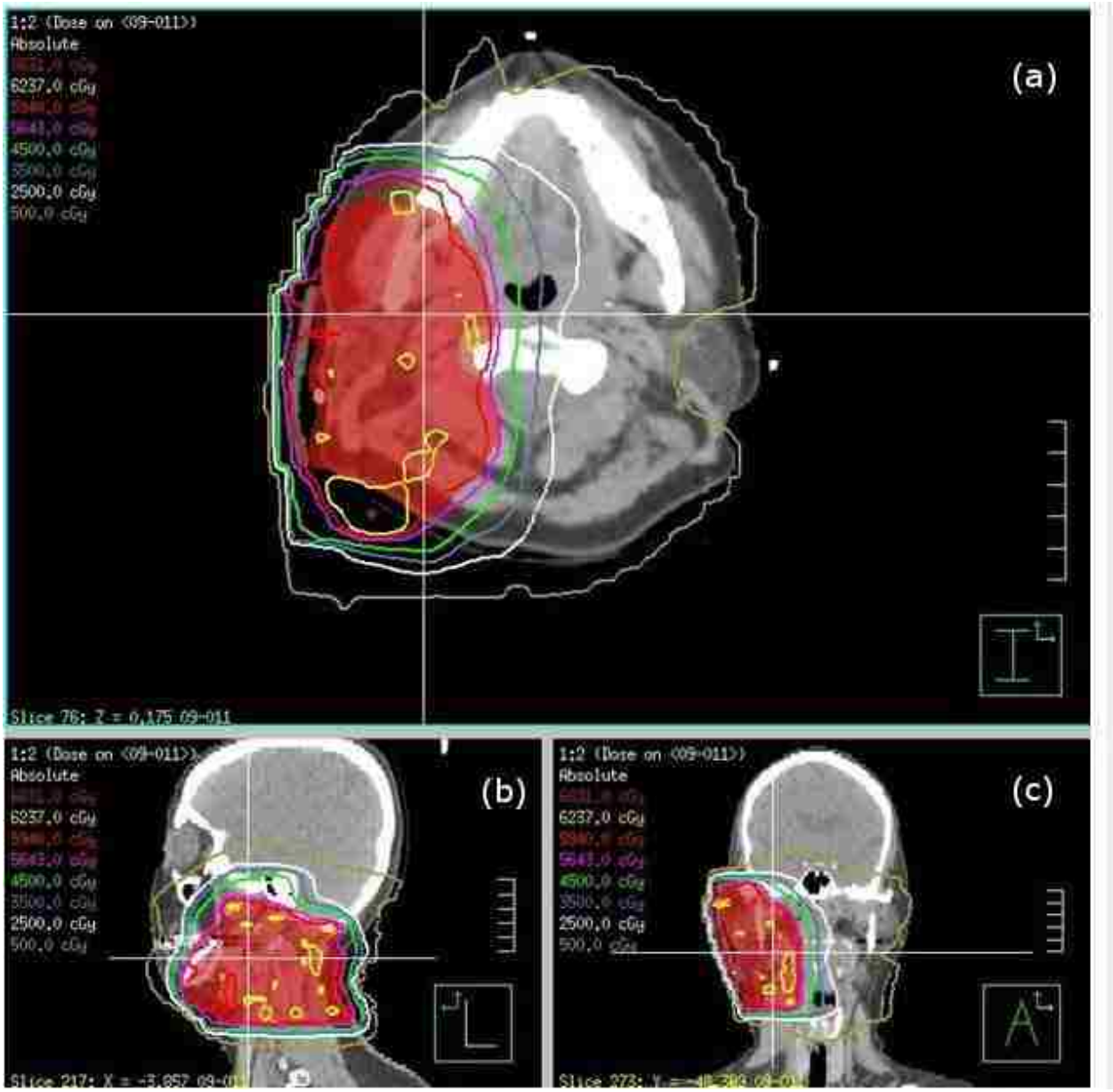

Figure 42 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 1:2 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

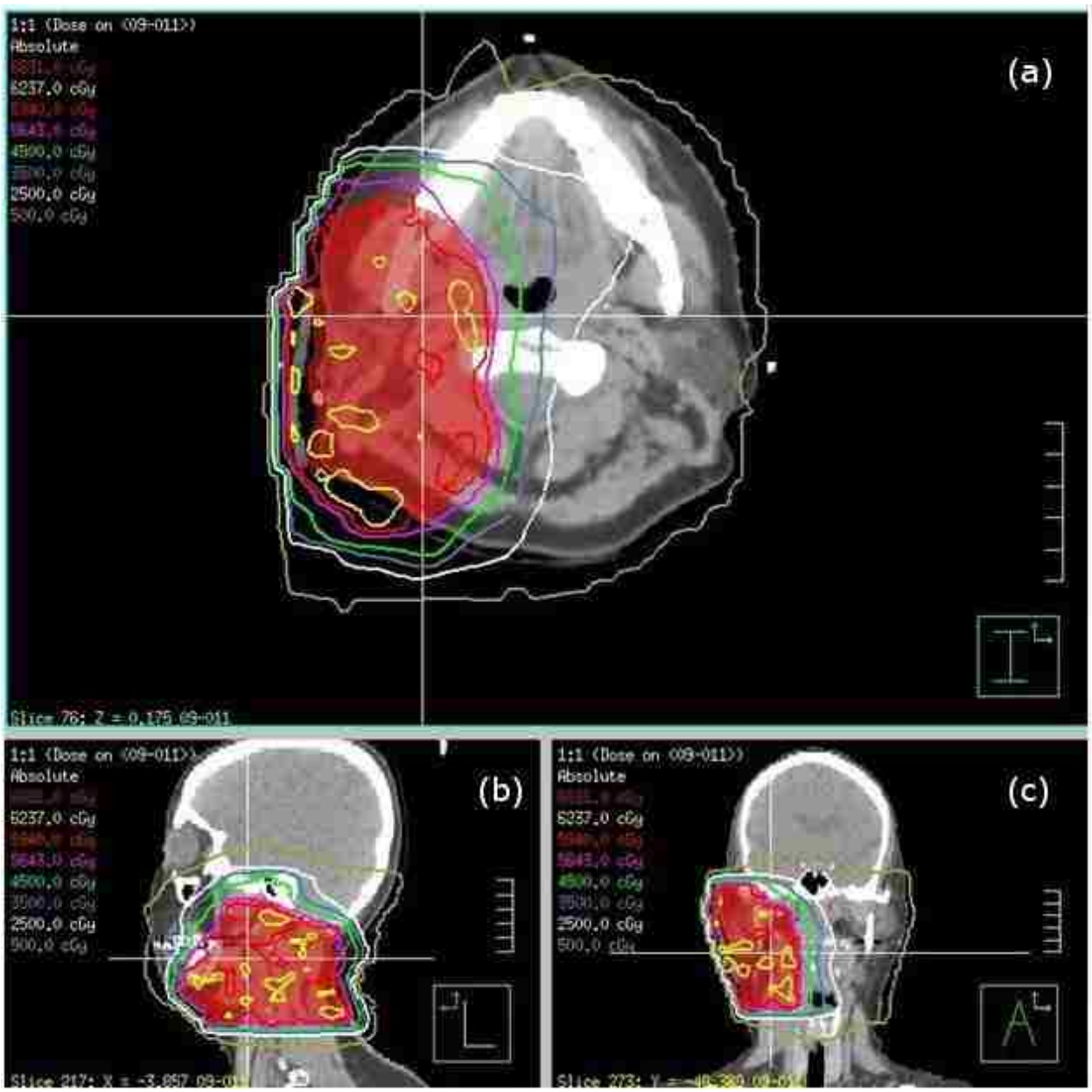

Figure 43 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 1:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

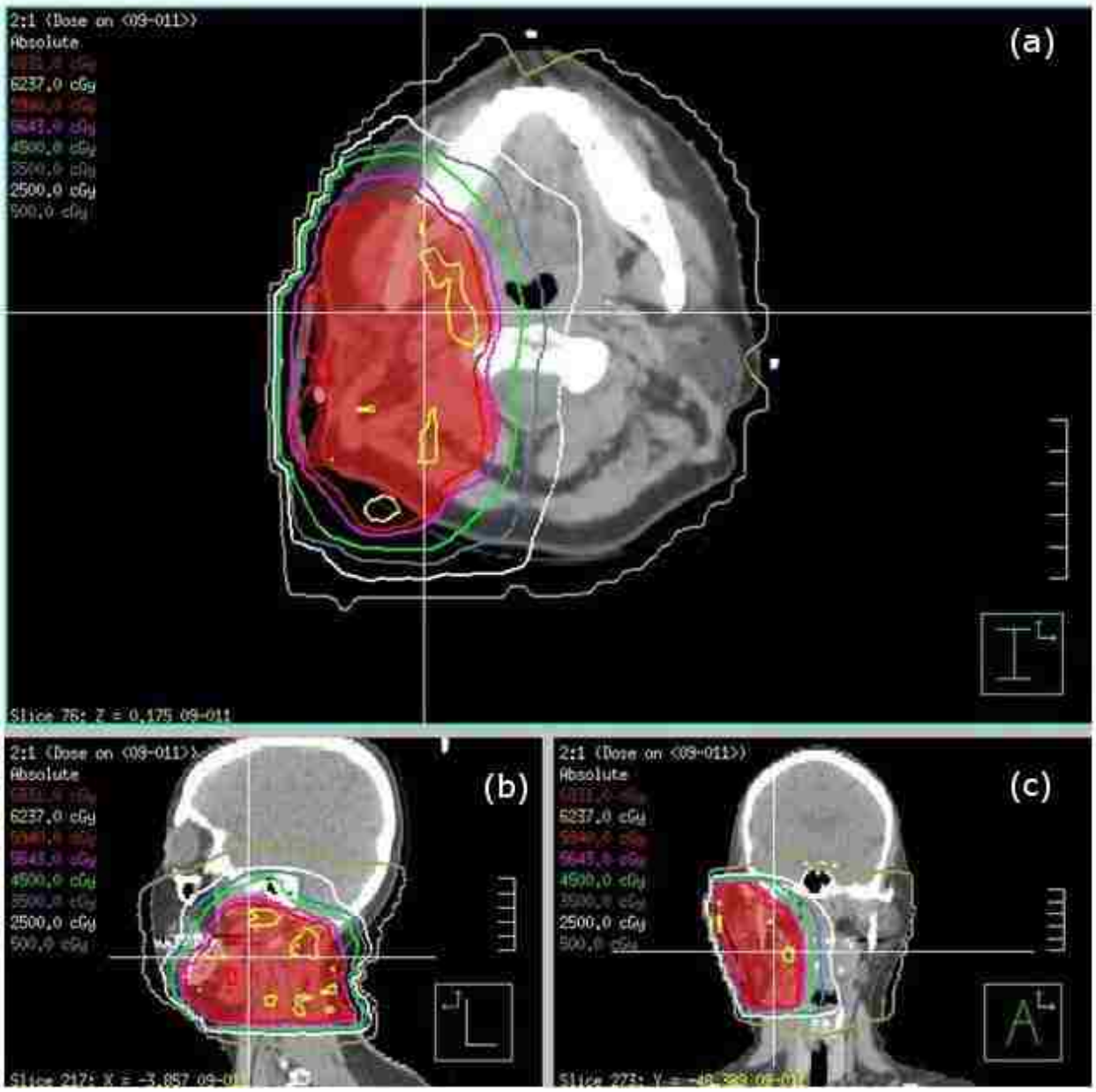

Figure 44 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for 2:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

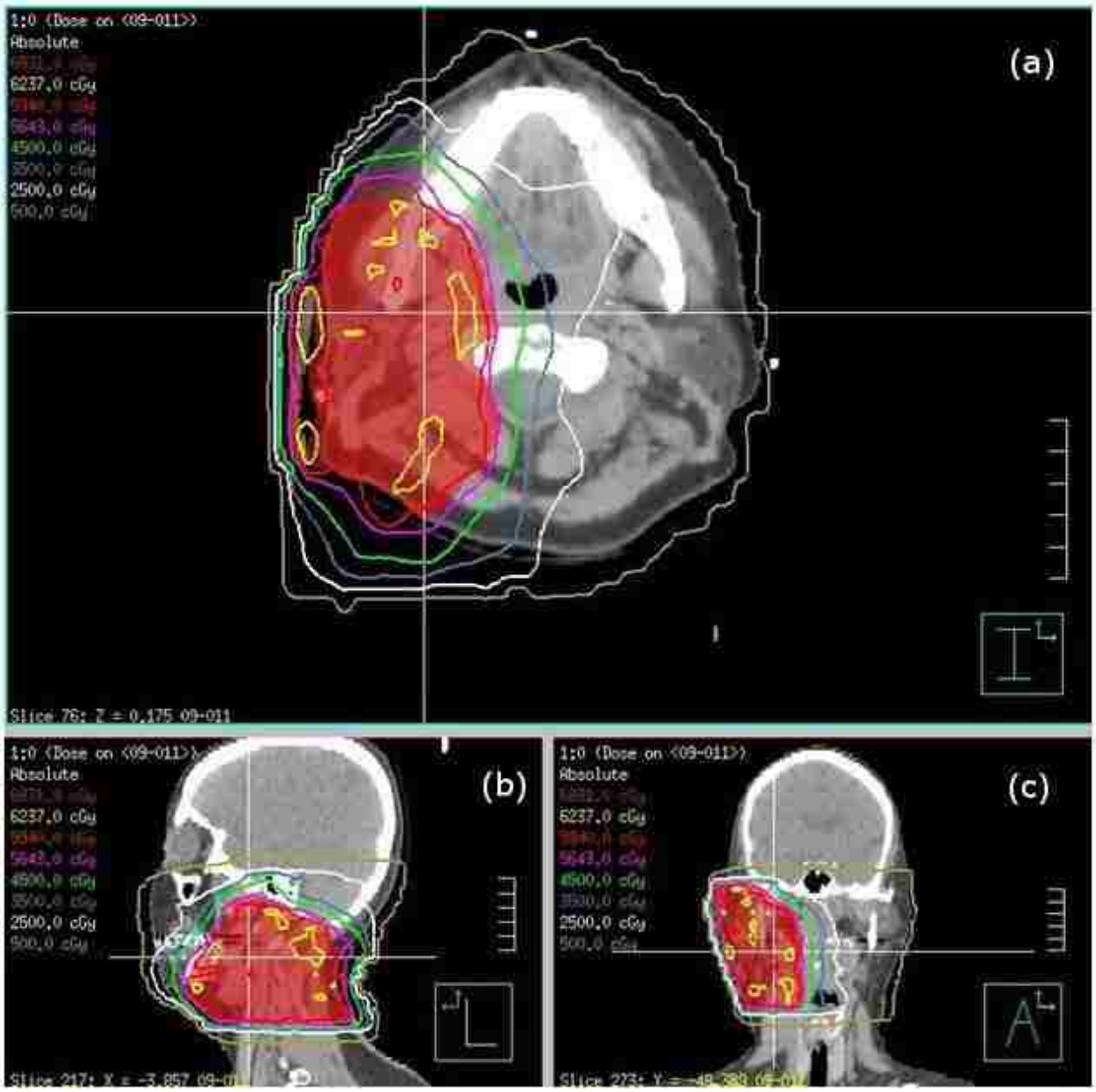

Figure 45 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for the IMRT plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

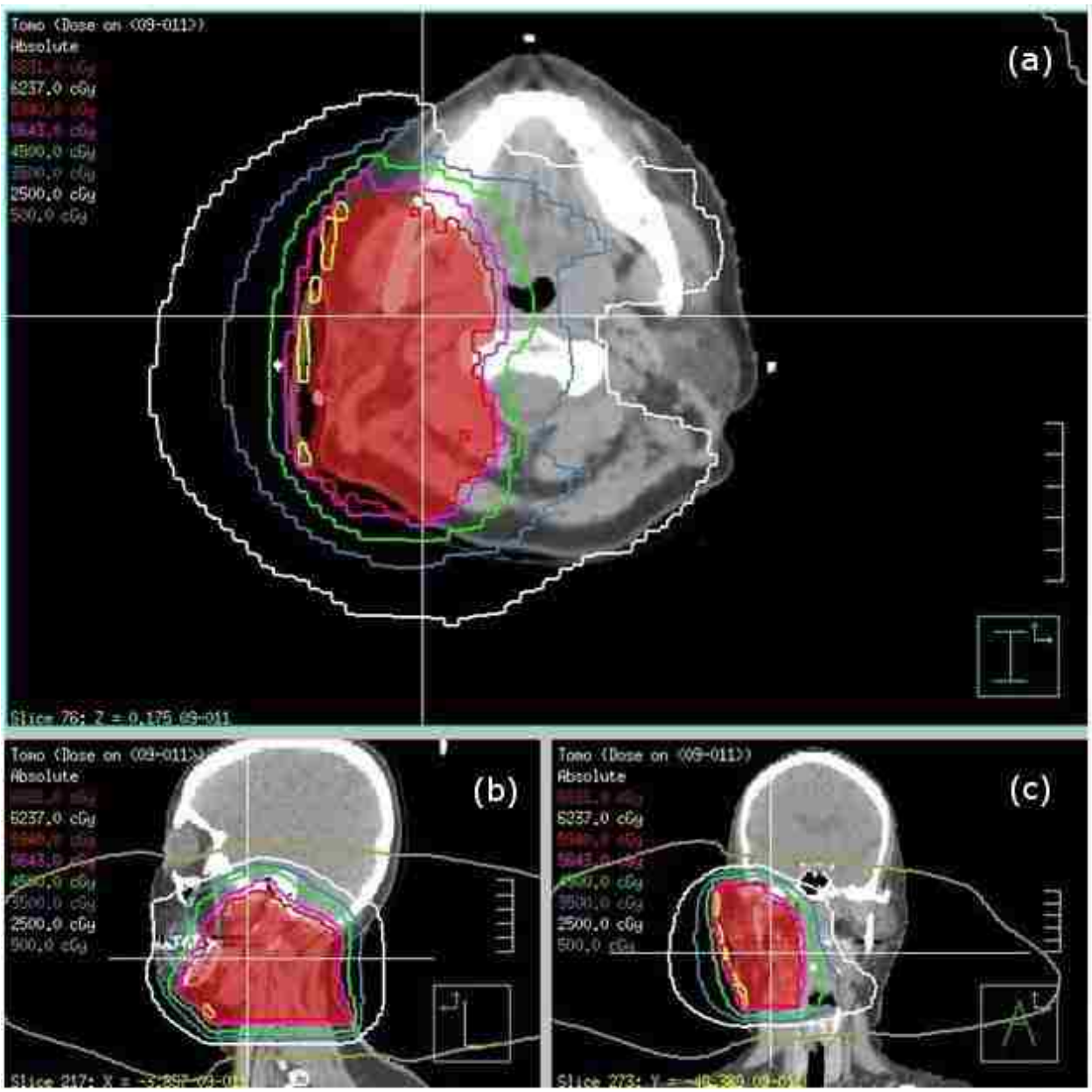

Figure 46 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 1 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

Patient 2

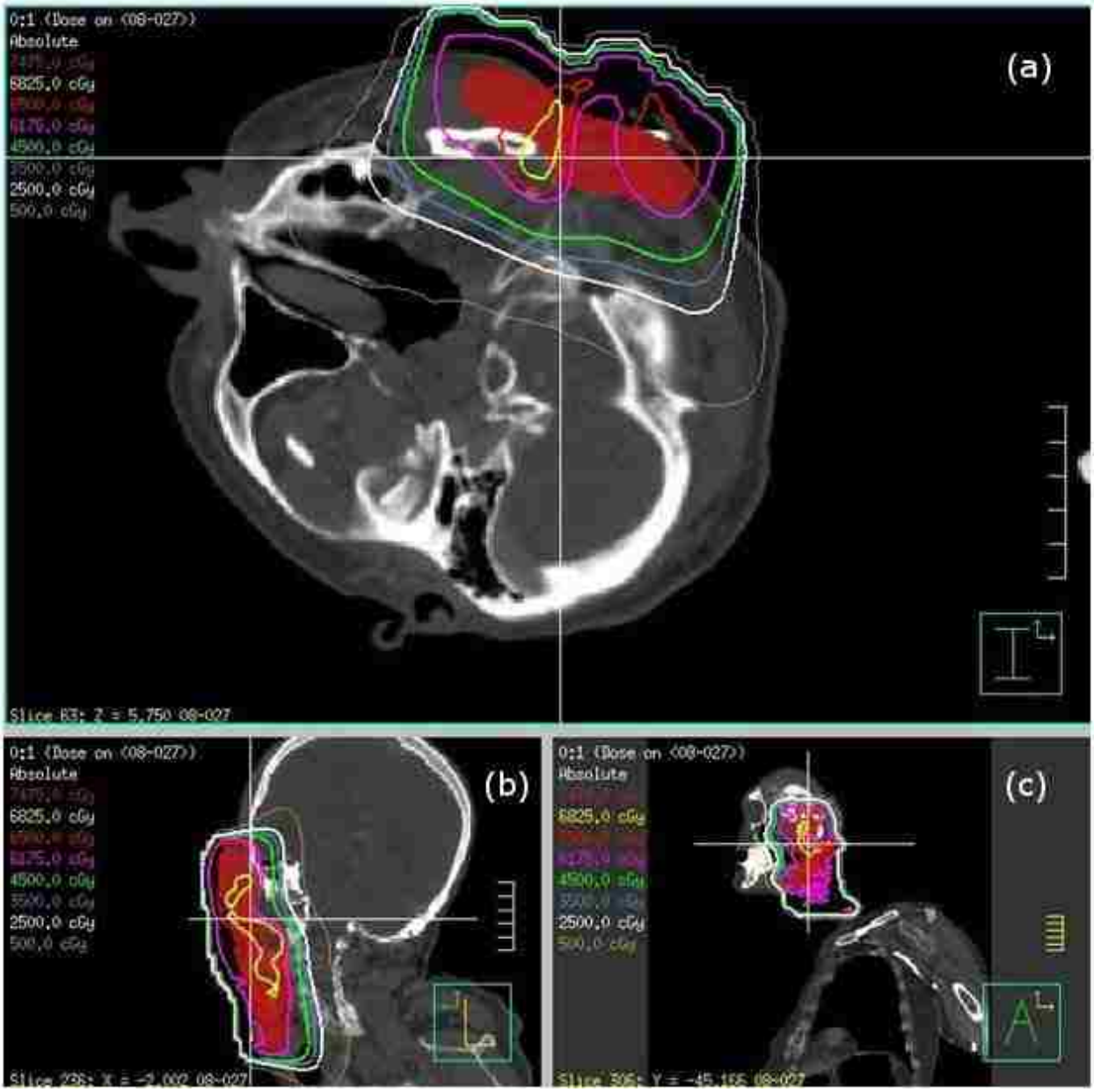

Figure 47 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 0:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

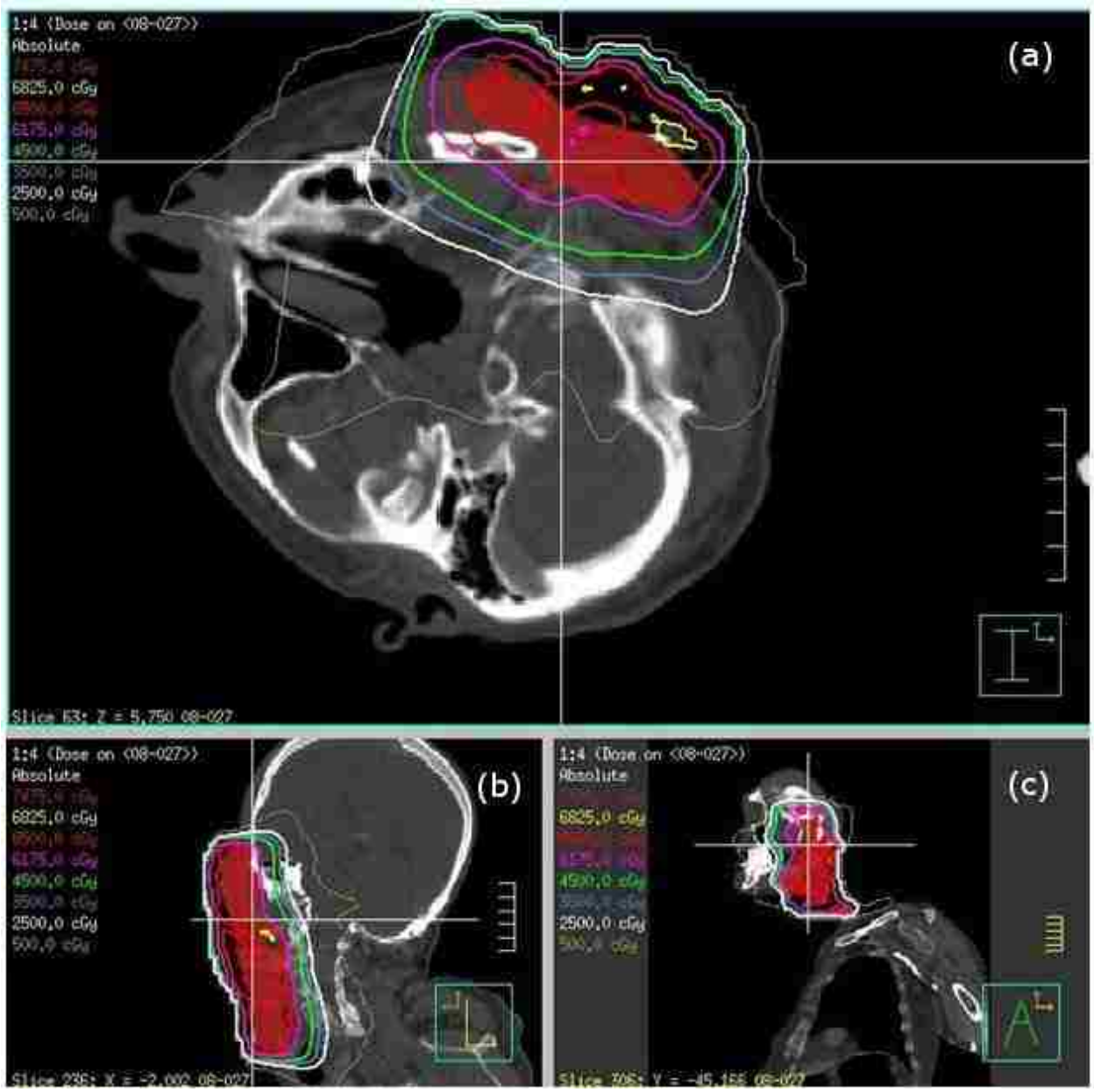

Figure 48 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 1:4 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

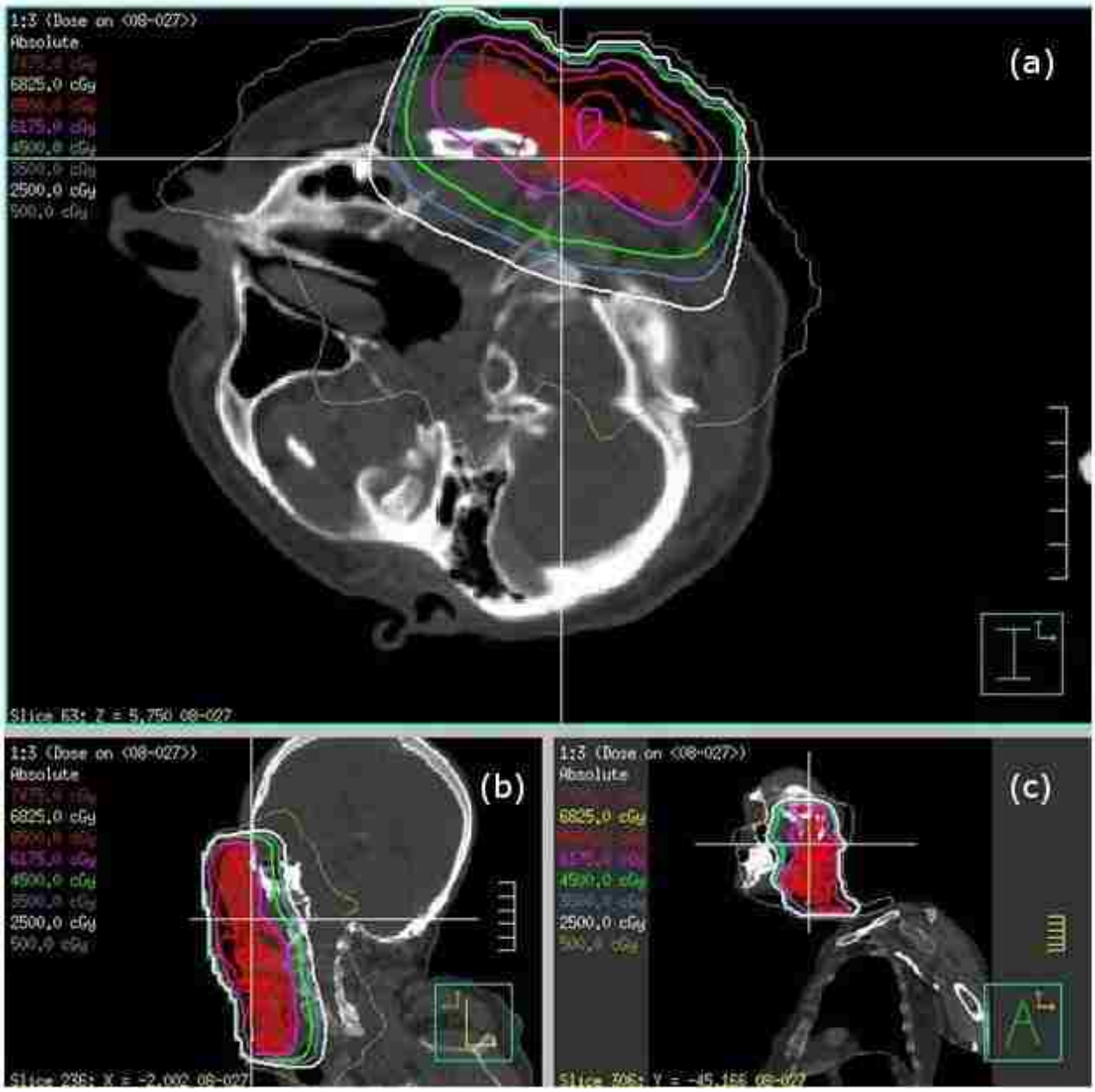

Figure 49 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 1:3 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

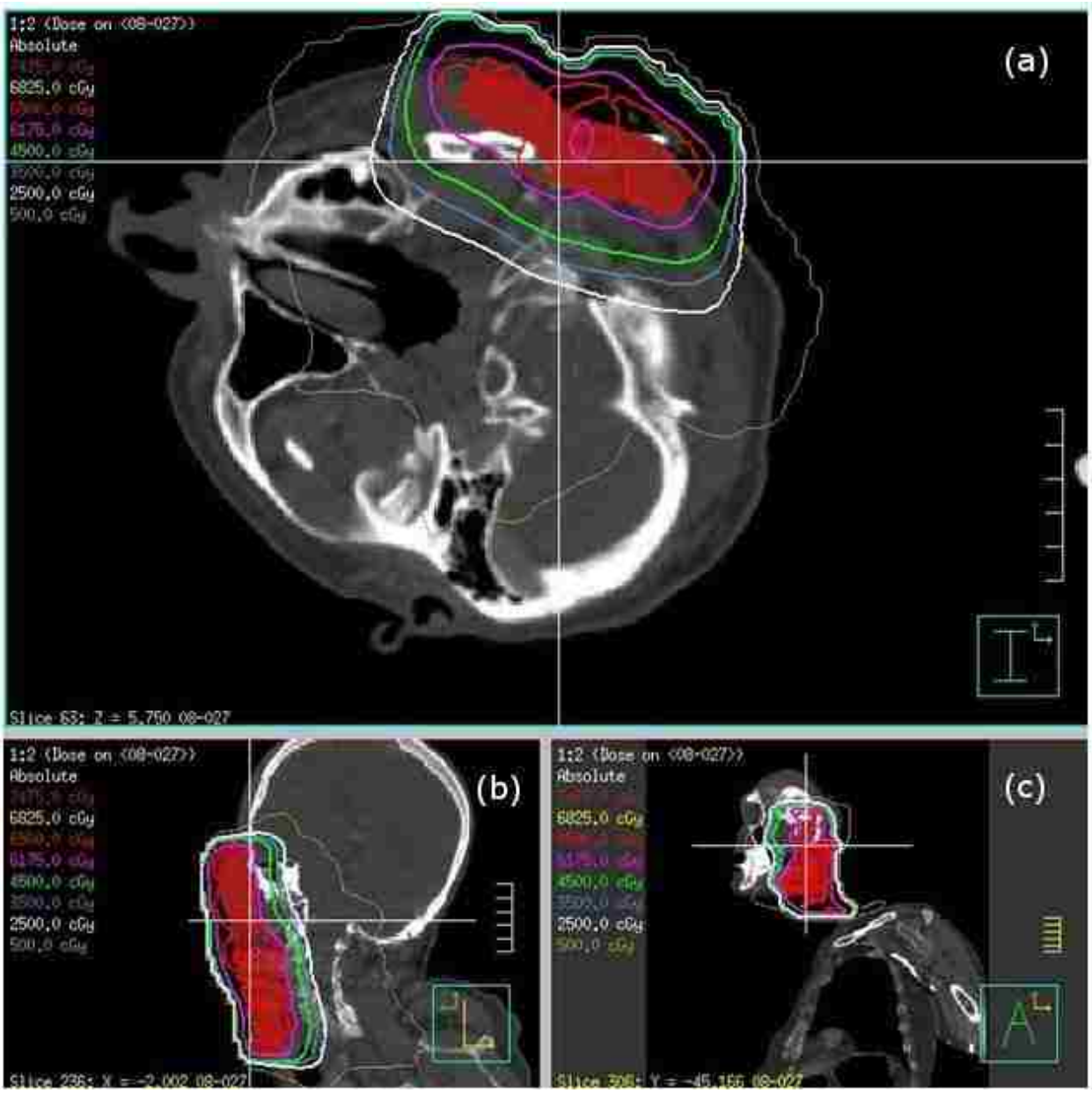

Figure 50 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 1:2 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

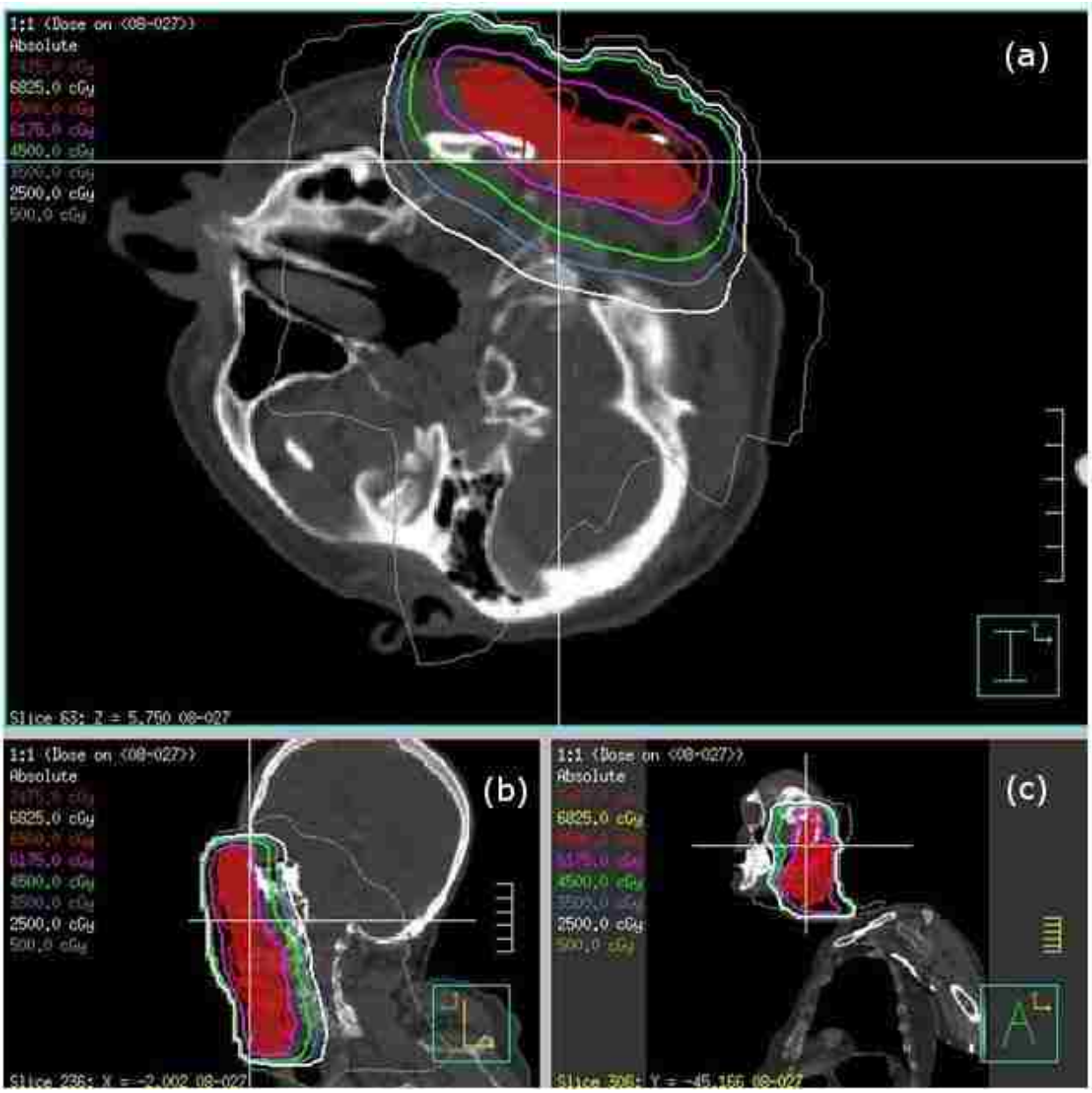

Figure 51 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 1:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

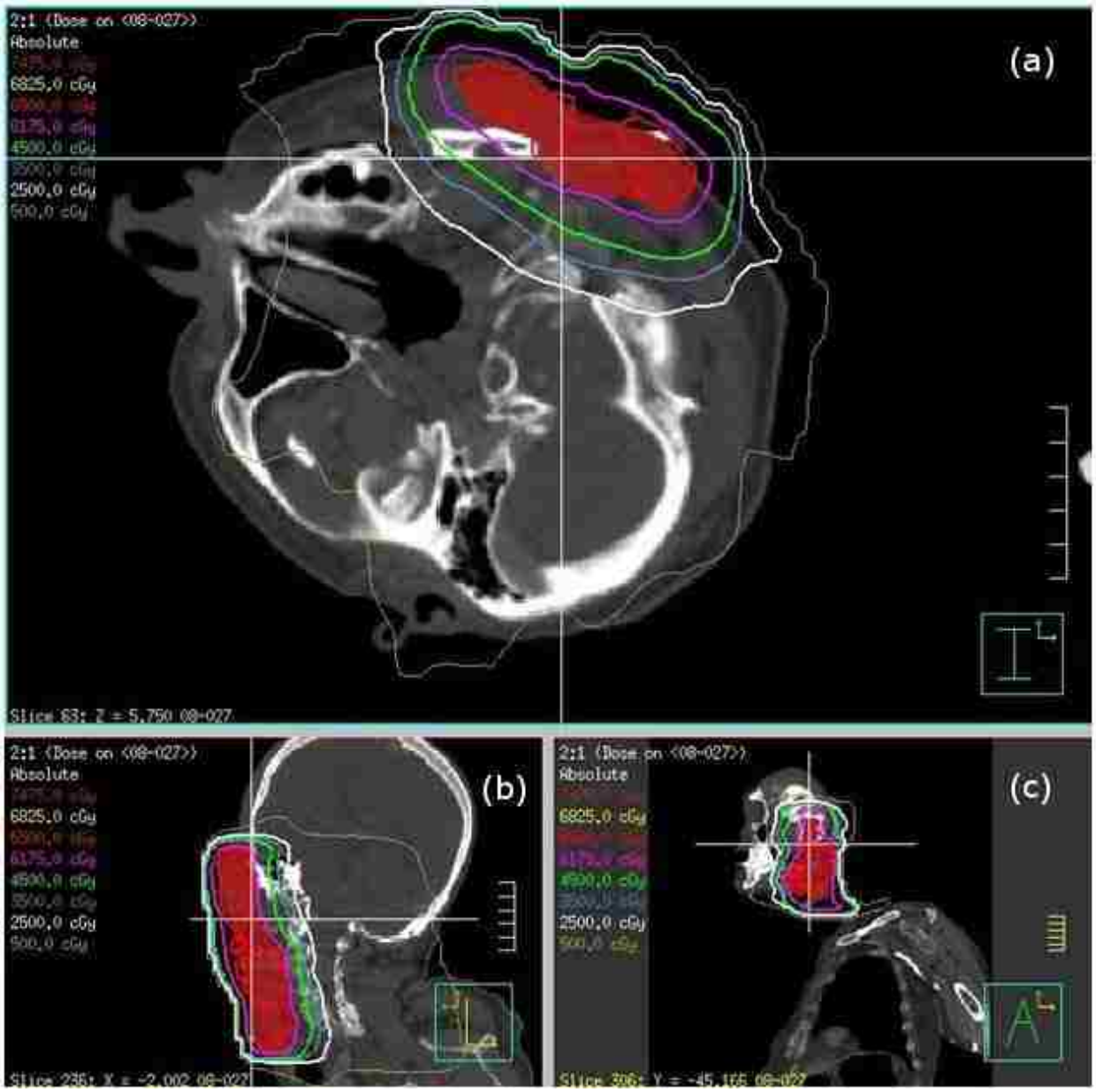

Figure 52 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for 2:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

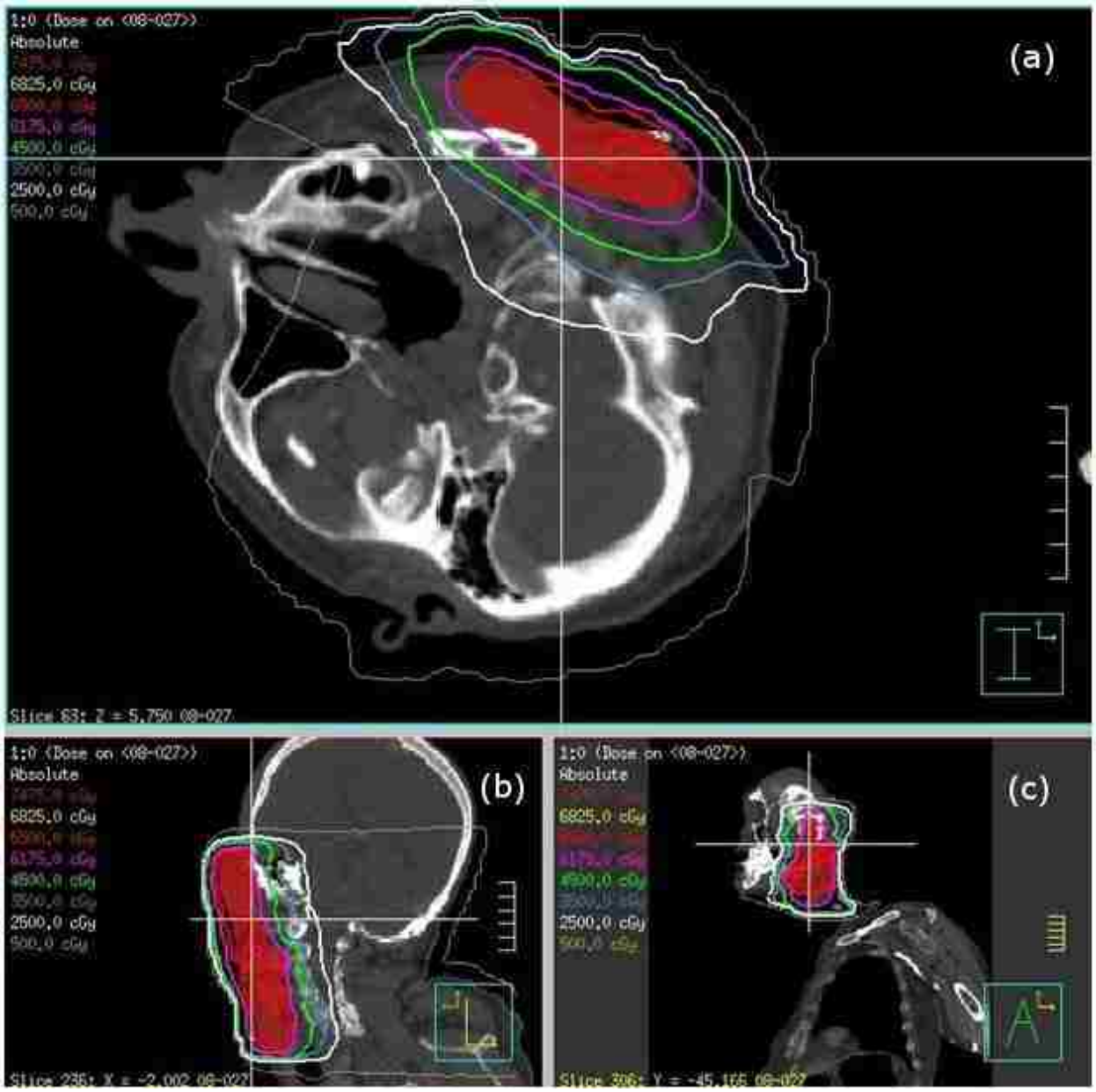

Figure 53 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for the IMRT plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

Figure 54 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 2 for the TomoTherapy plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

Patient 3

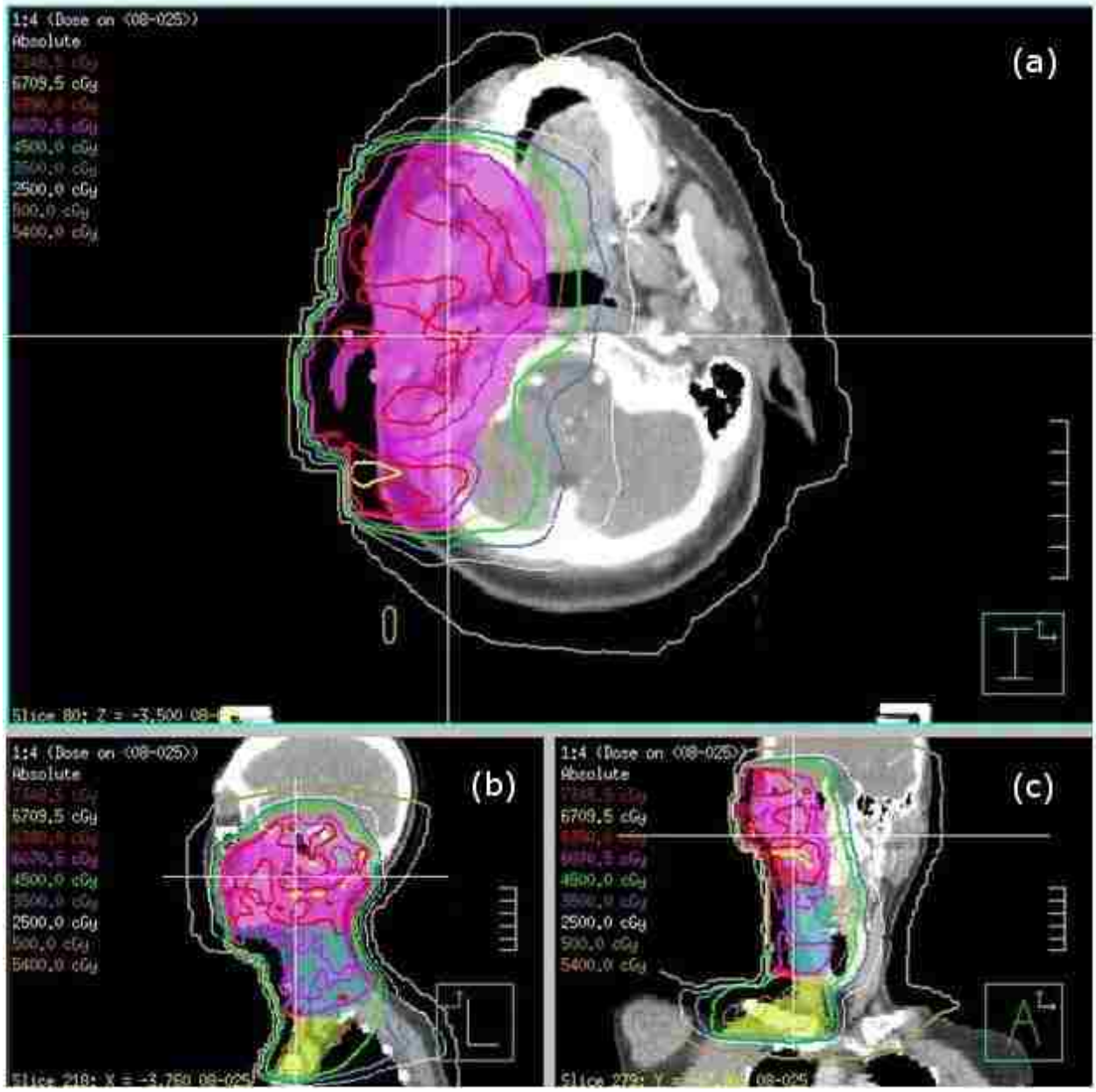

Figure 55 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for 1:4 ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

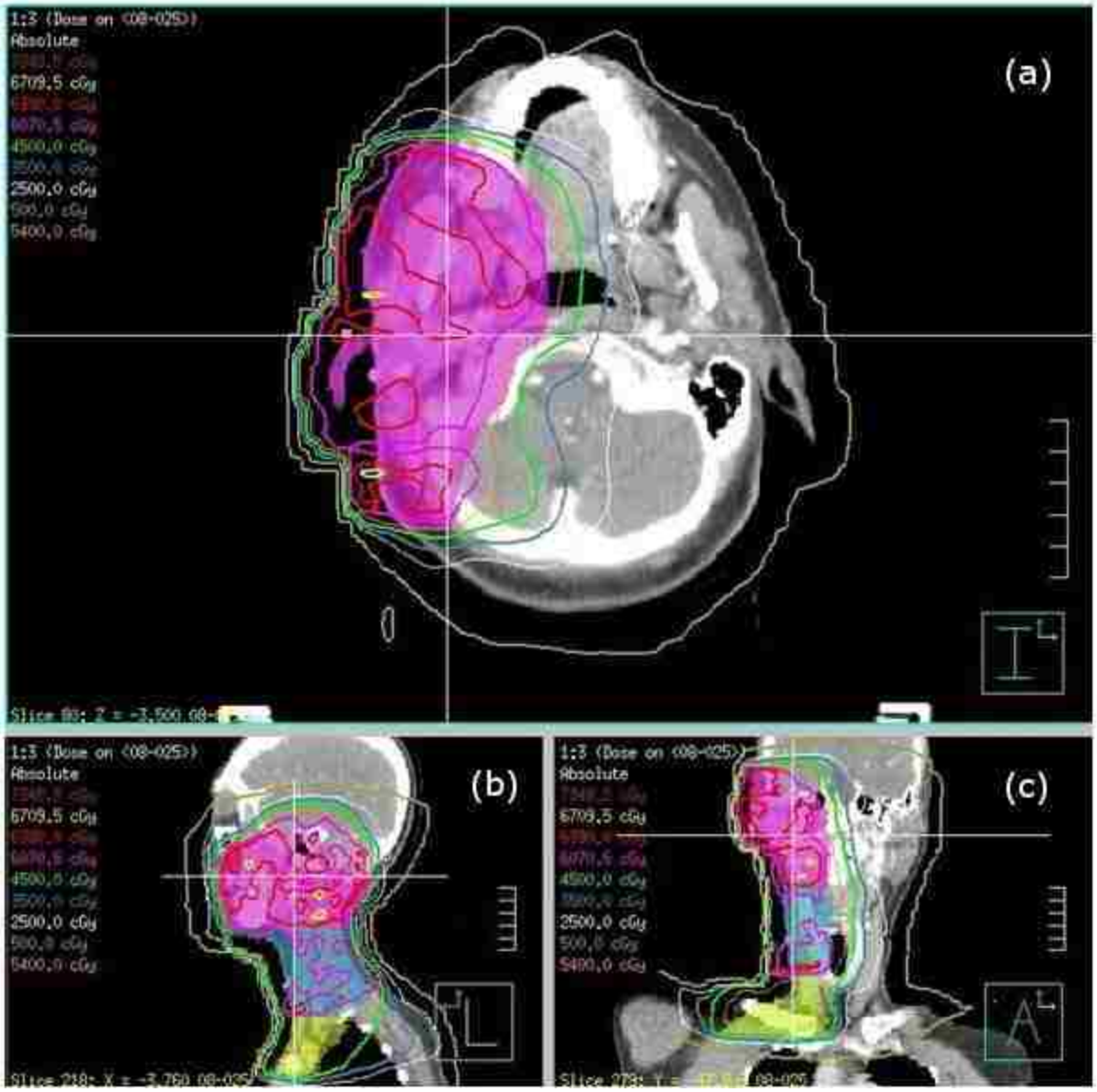

Figure 56 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for 1:3 ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

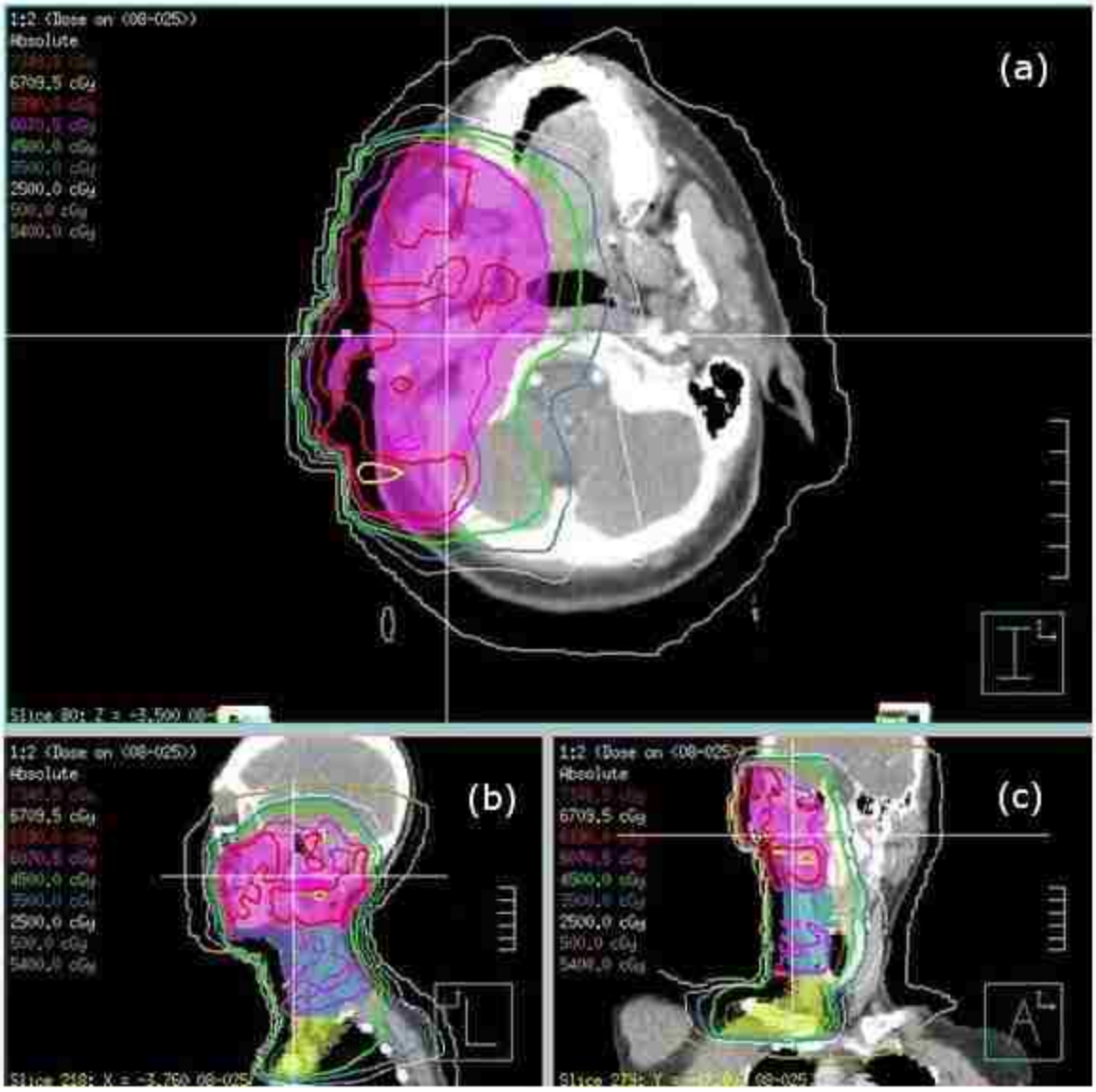

Figure 57 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for 1:2 ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

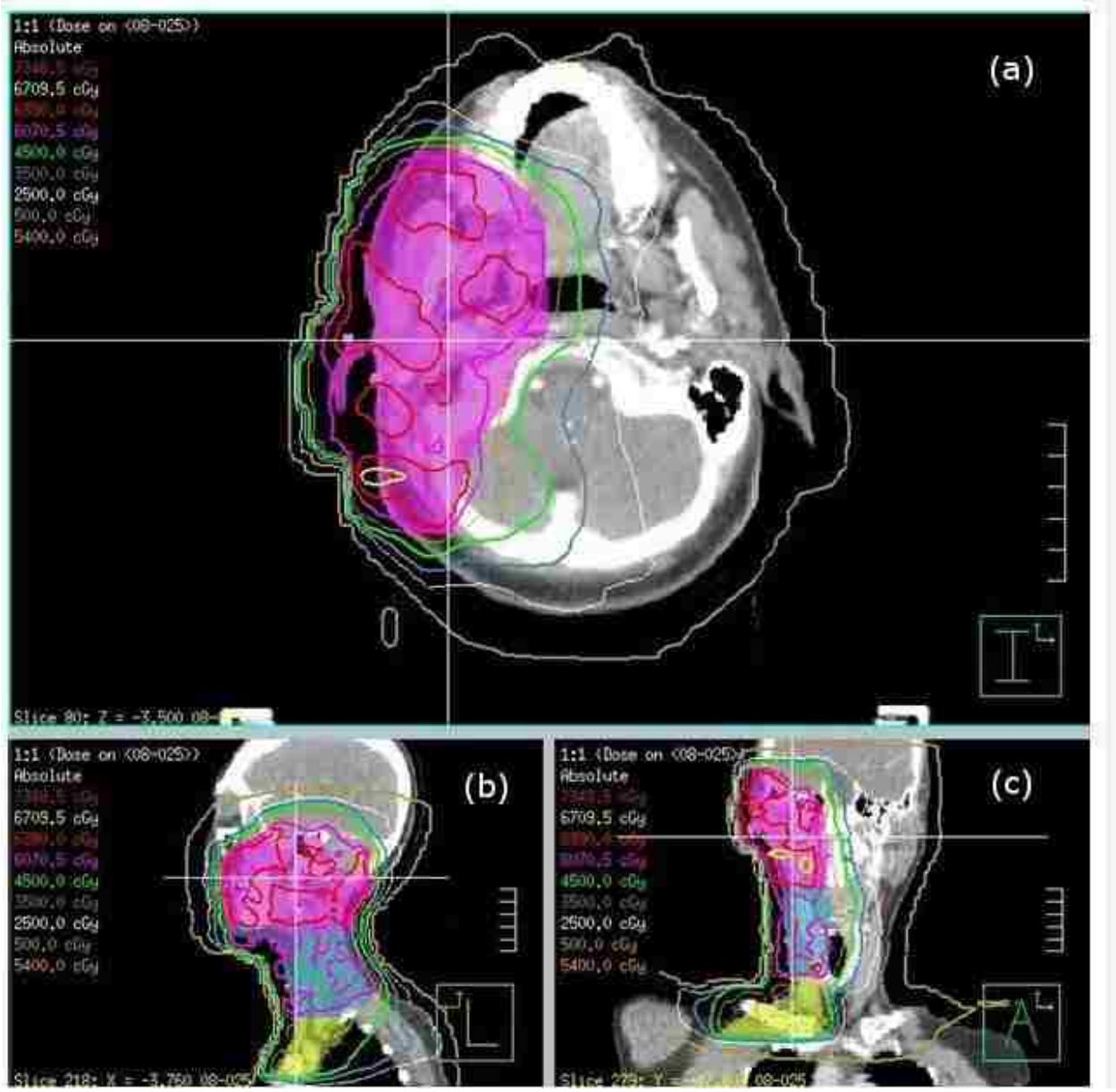

Figure 58 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for 1:1 ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

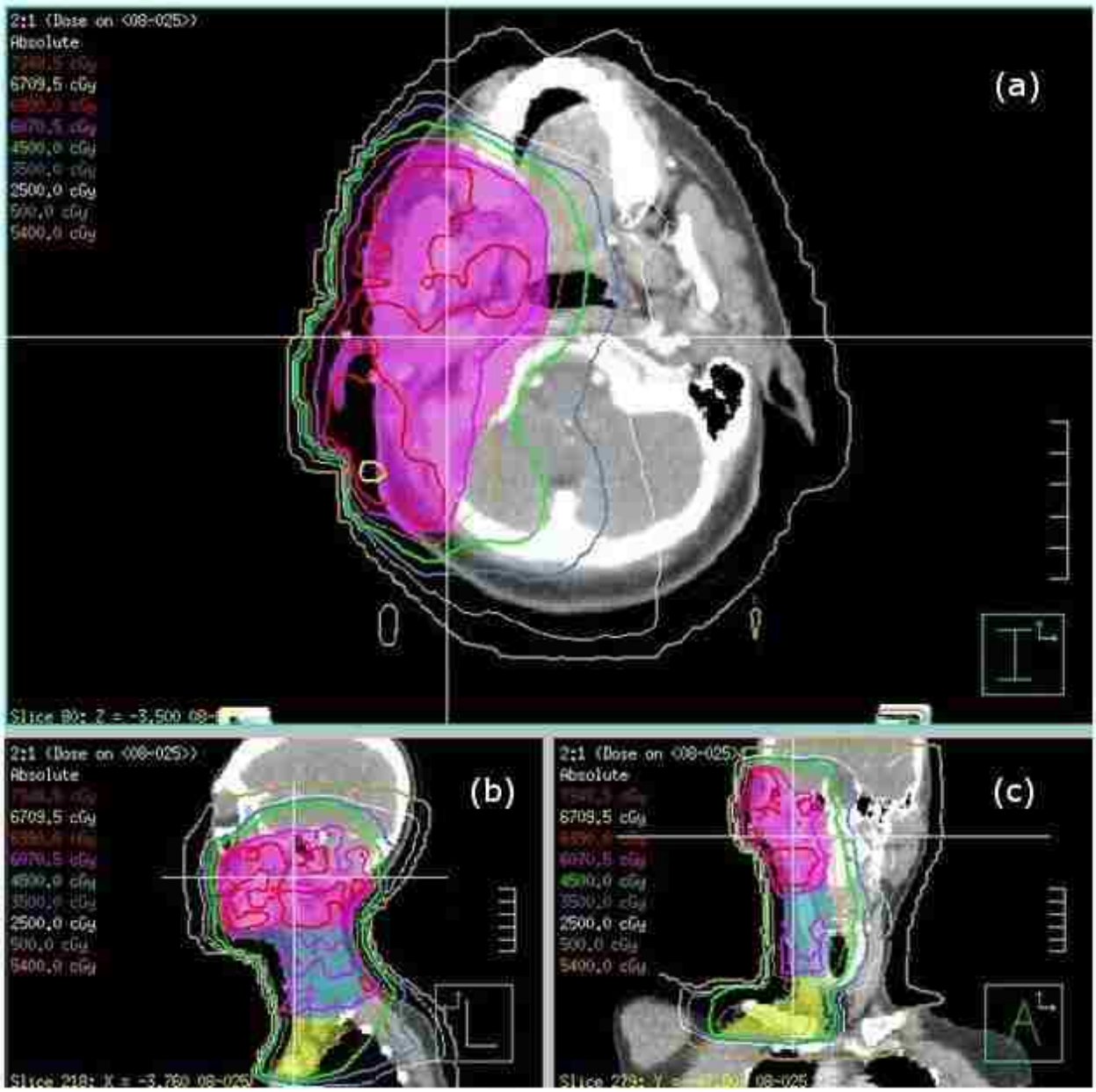

Figure 59 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for 2:1 ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

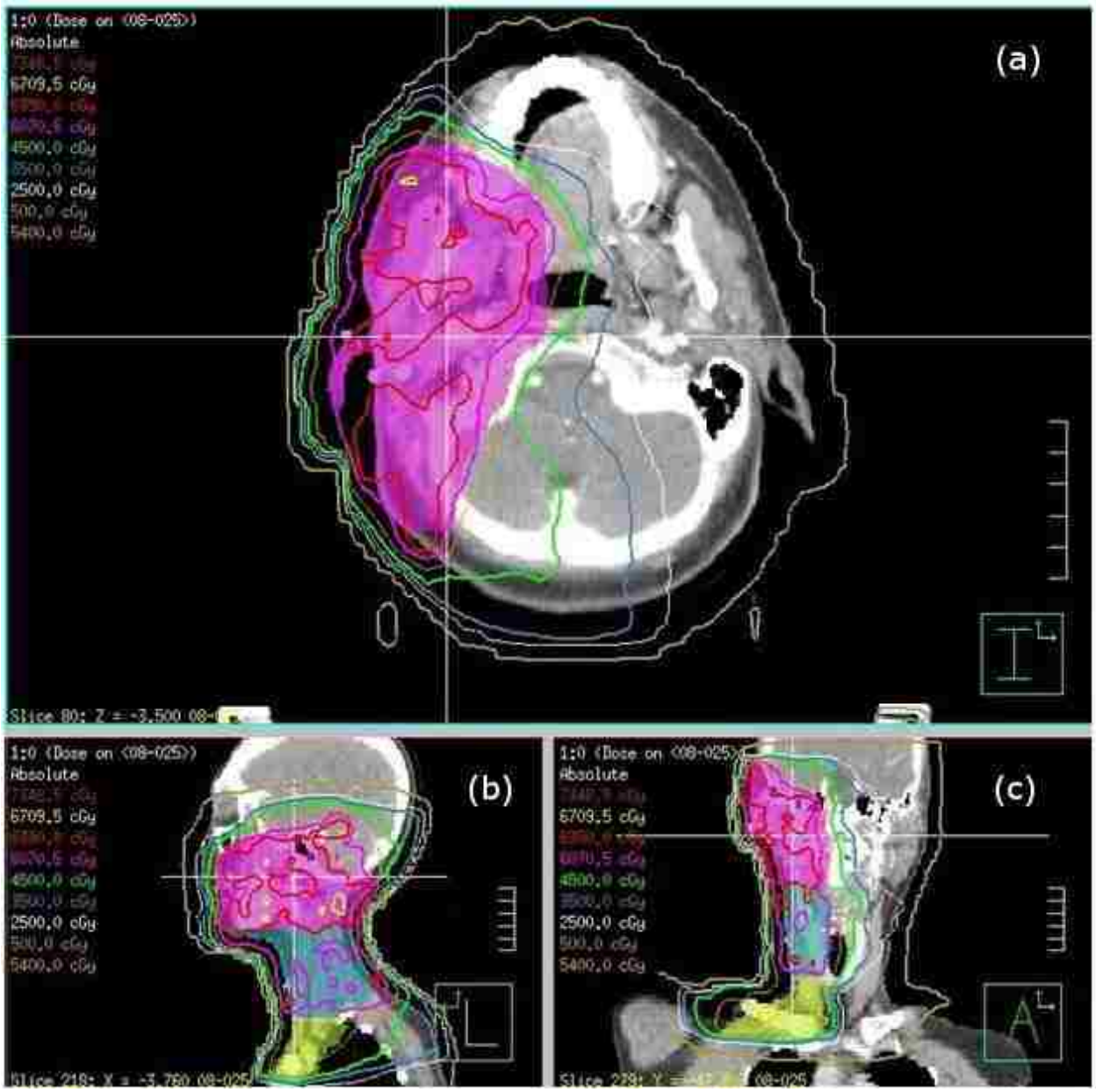

Figure 60 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for the IMRT plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

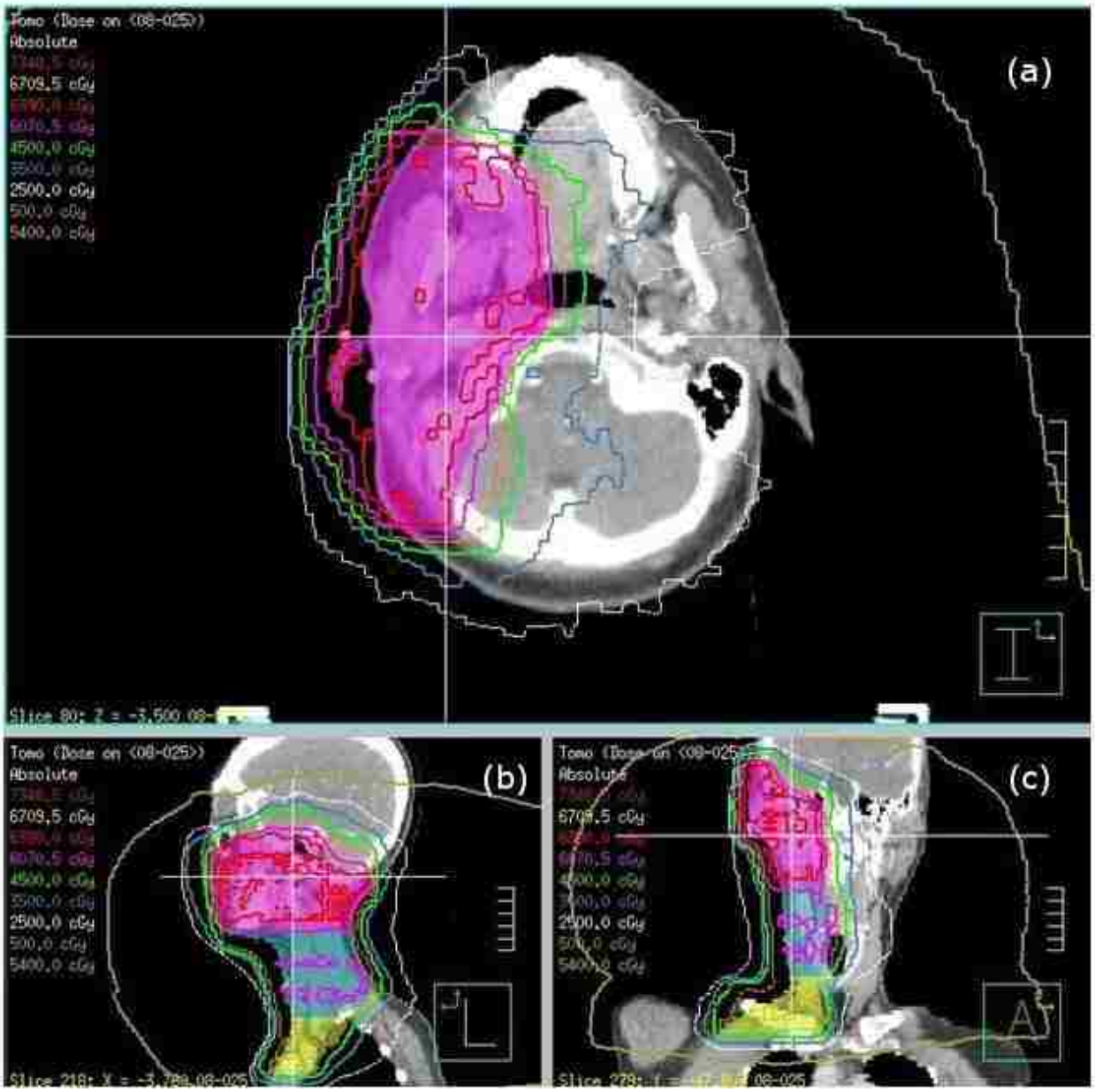

Figure 61 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 3 for the TomoTherapy ratio plan. The white crosshair indicates the position of the planes shown. PTVs are shown in colorwash. Primary PTV, purple; PTV60, teal; PTV54, yellow

Patient 4

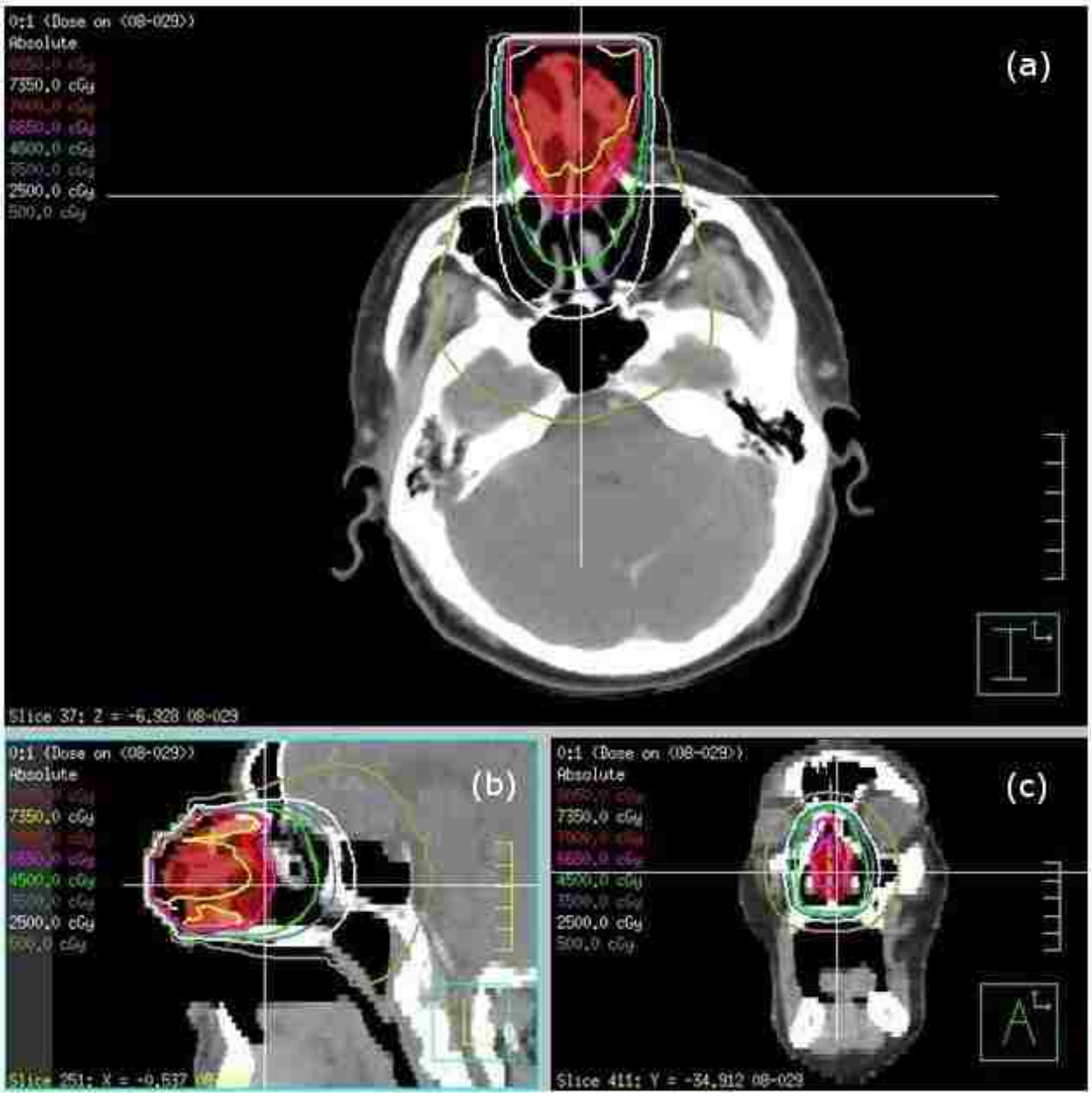

Figure 62 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 0:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

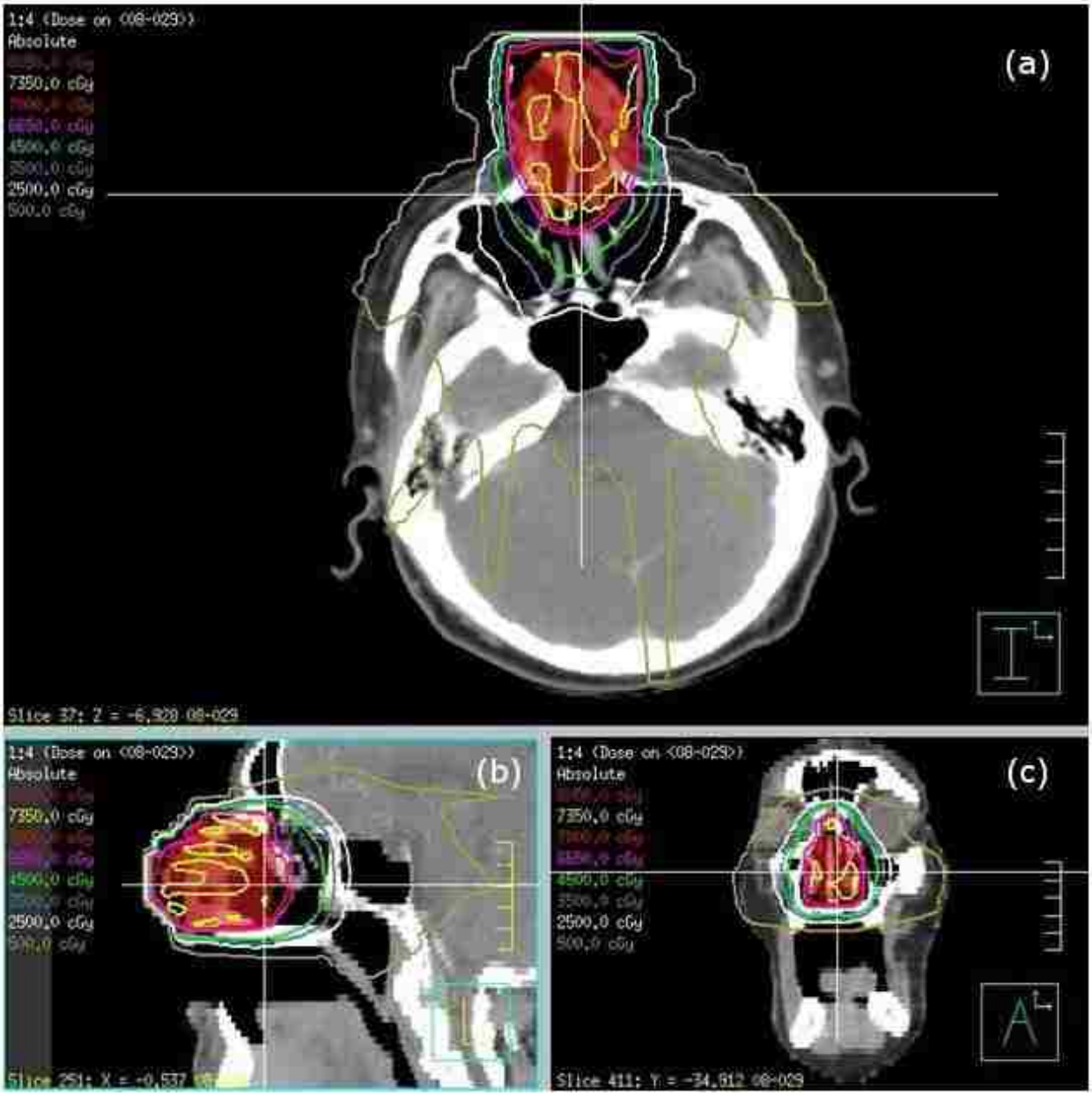

Figure 63 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 1:4 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

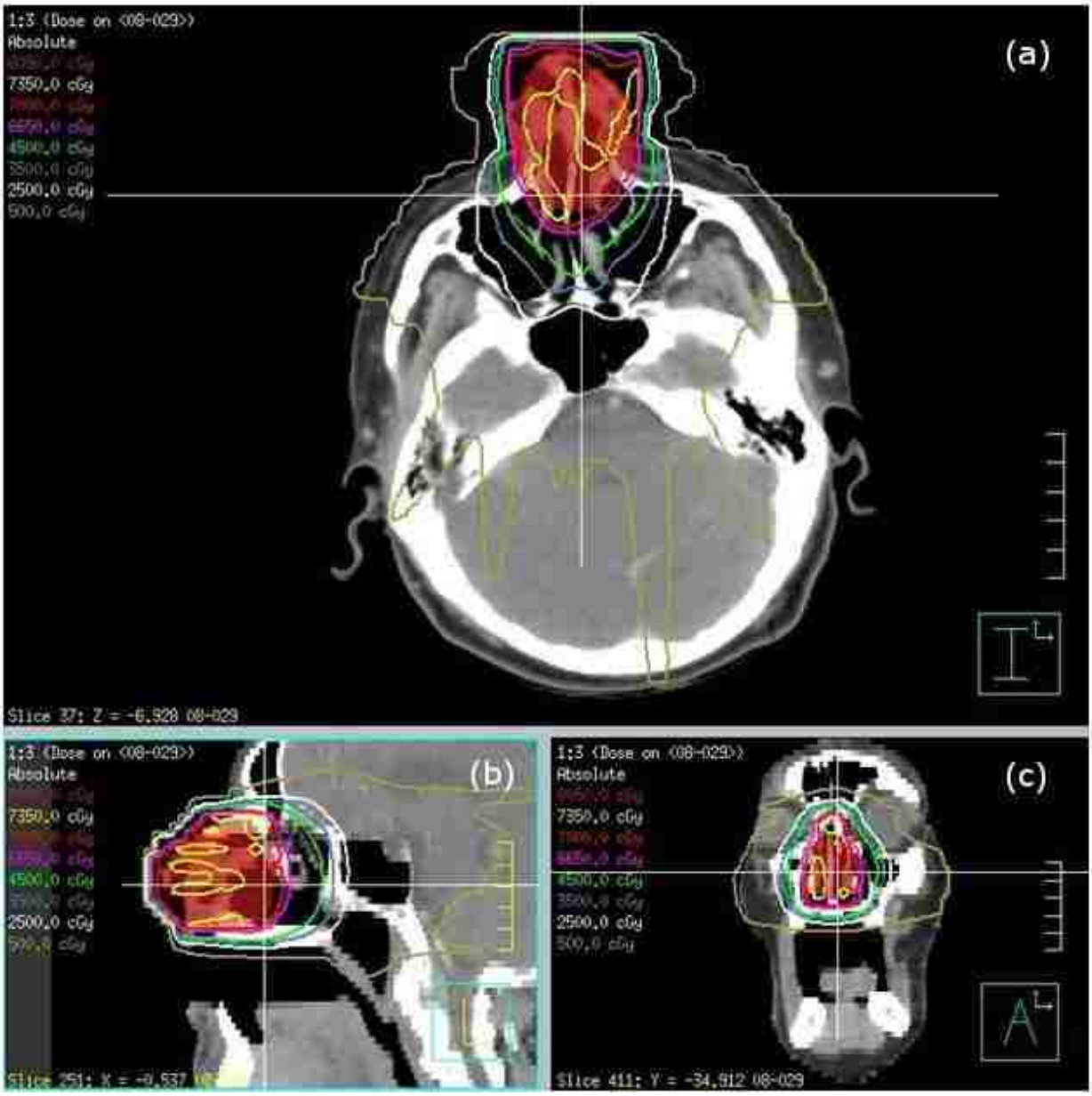

Figure 64 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 1:3 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

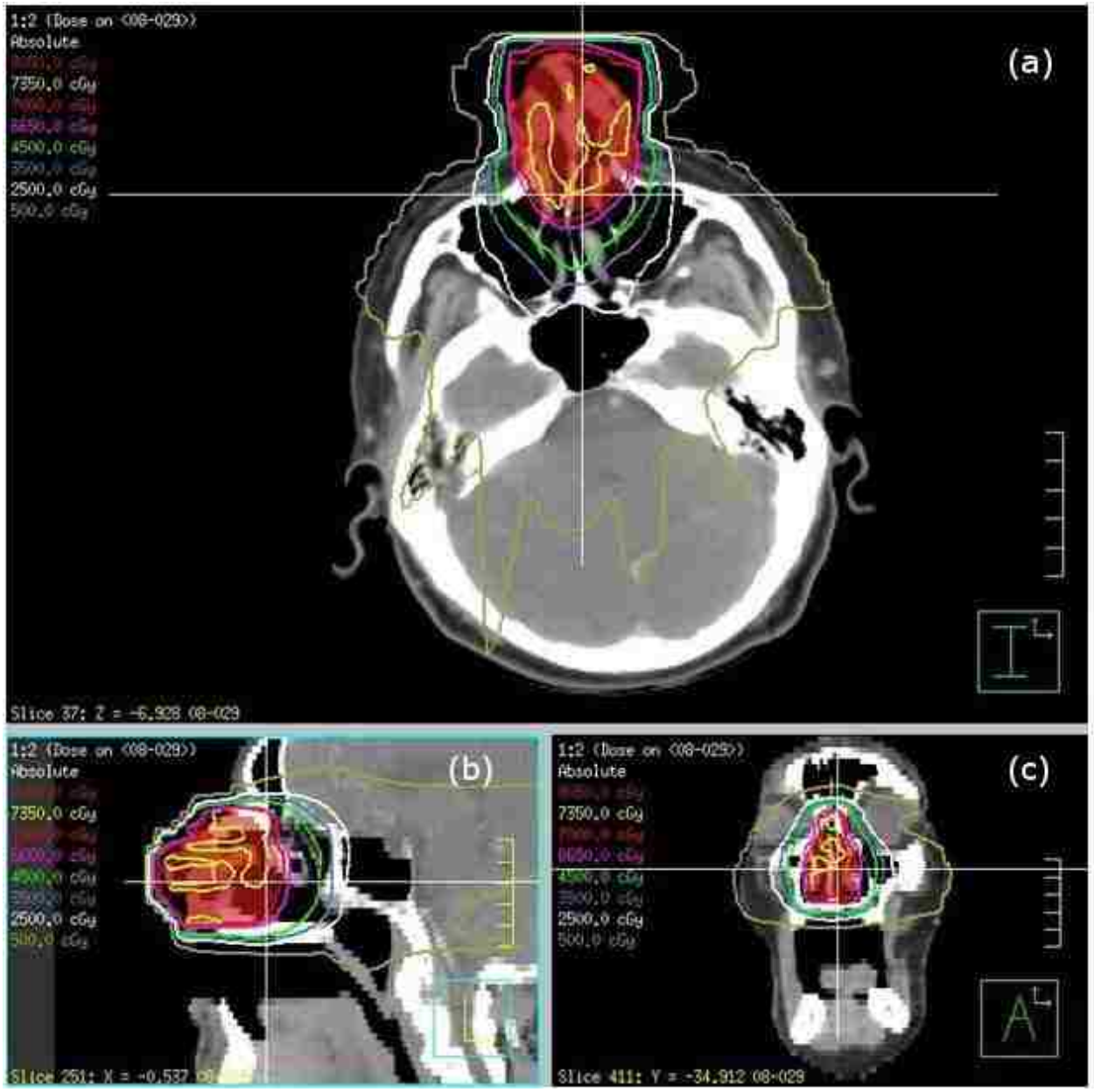

Figure 65 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 1:2 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

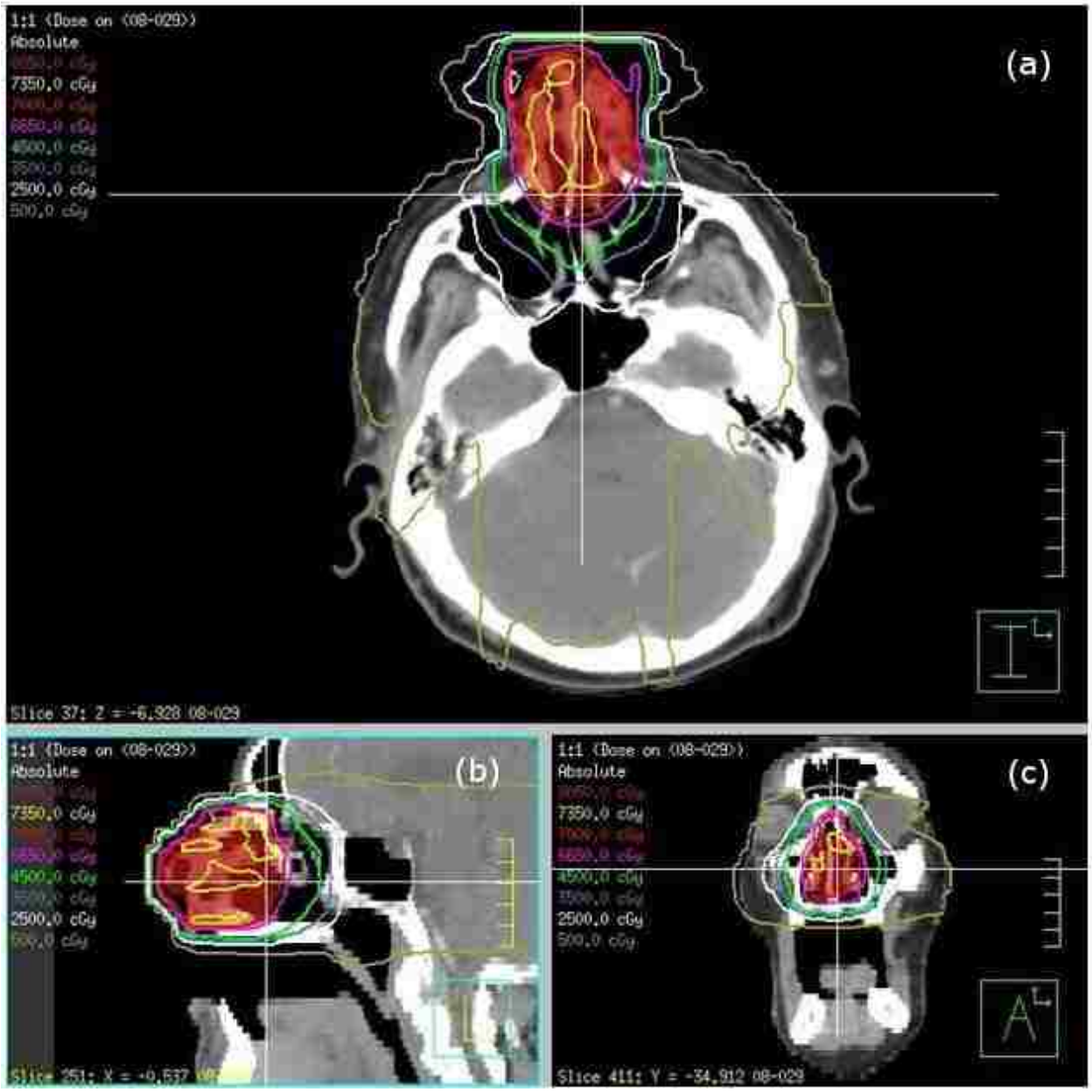

Figure 66 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 1:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

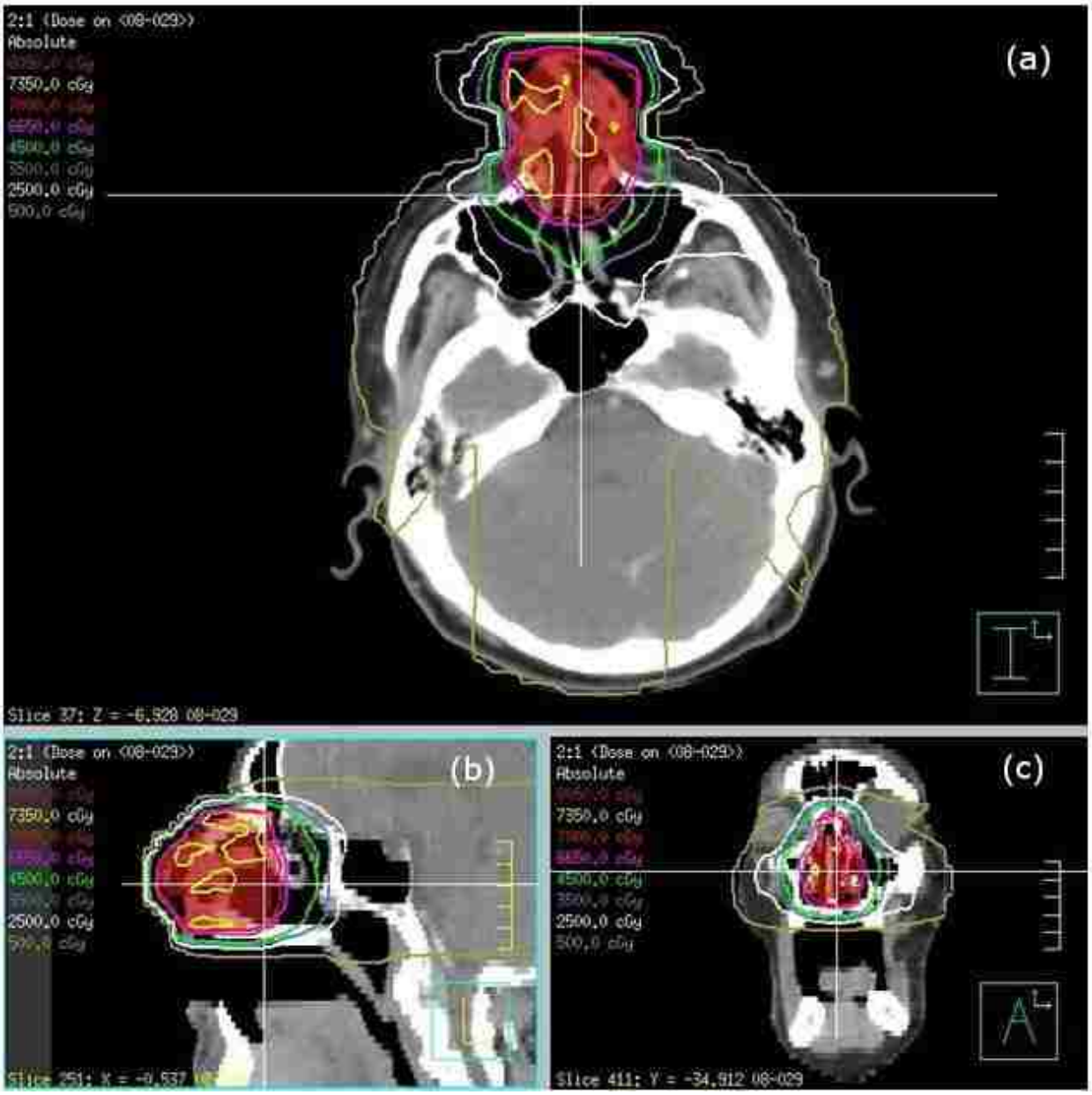

Figure 67 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for 2:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

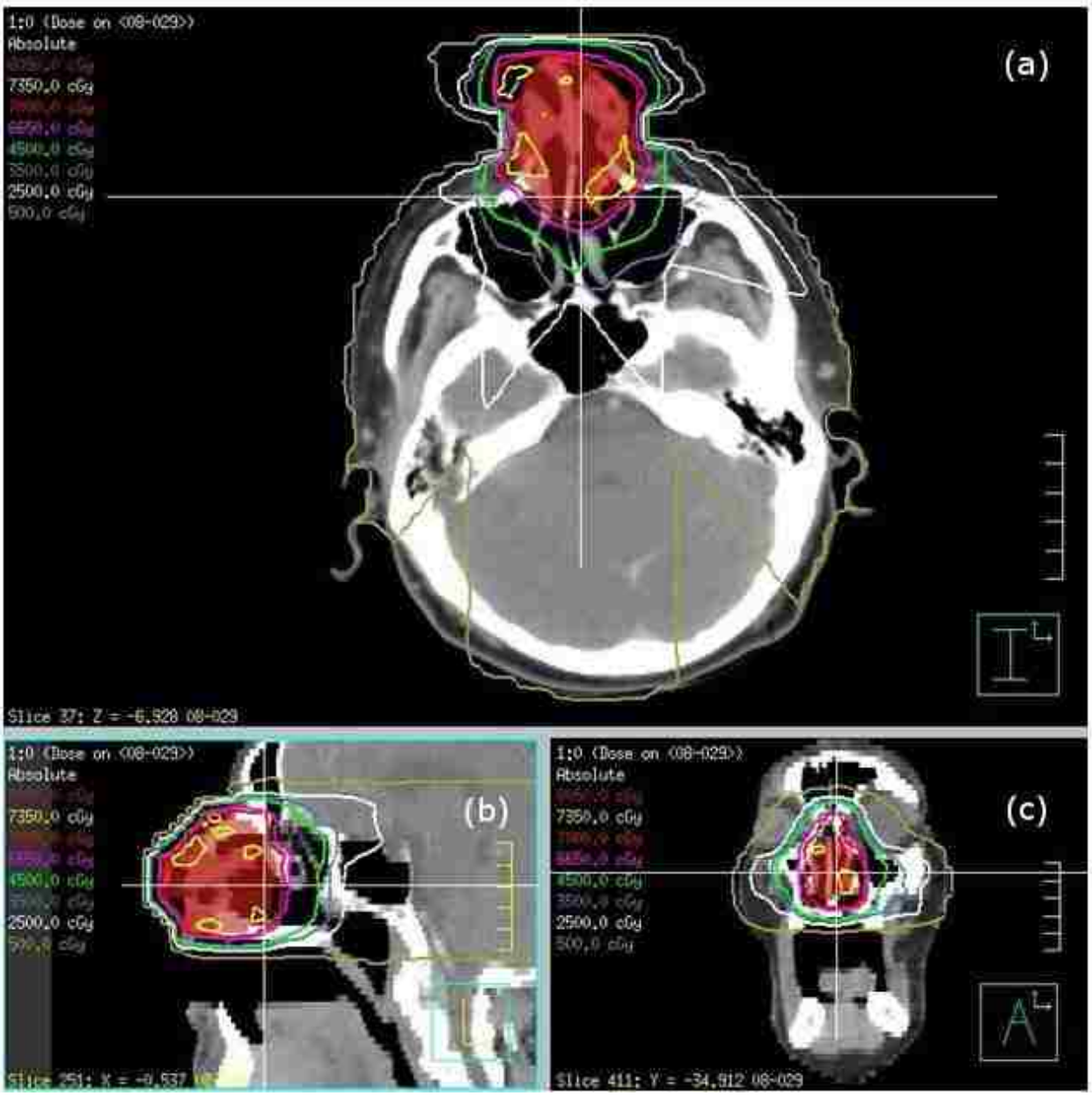

Figure 68 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for the IMRT plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

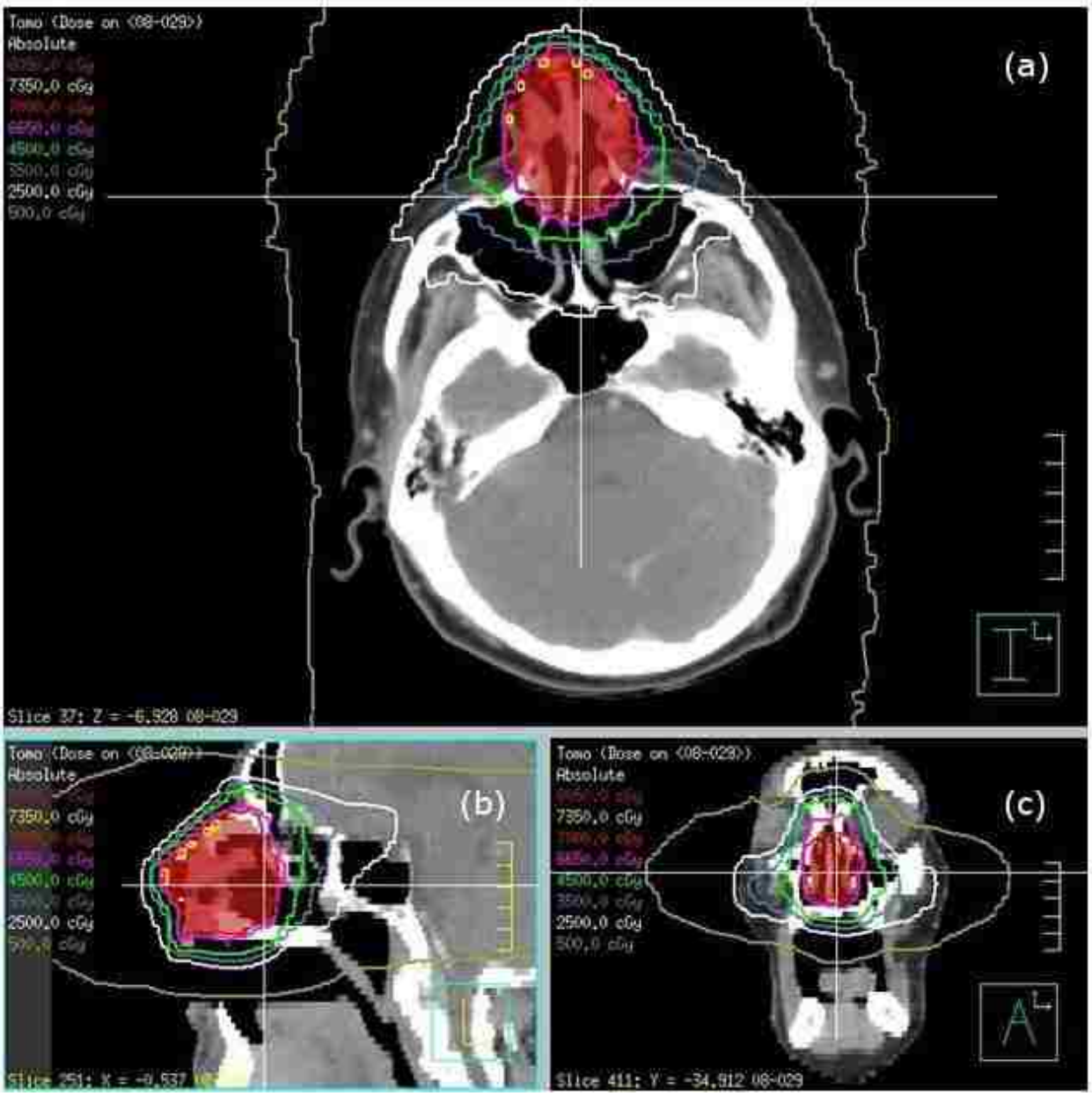

Figure 69 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 4 for the TomoTherapy ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

Patient 5

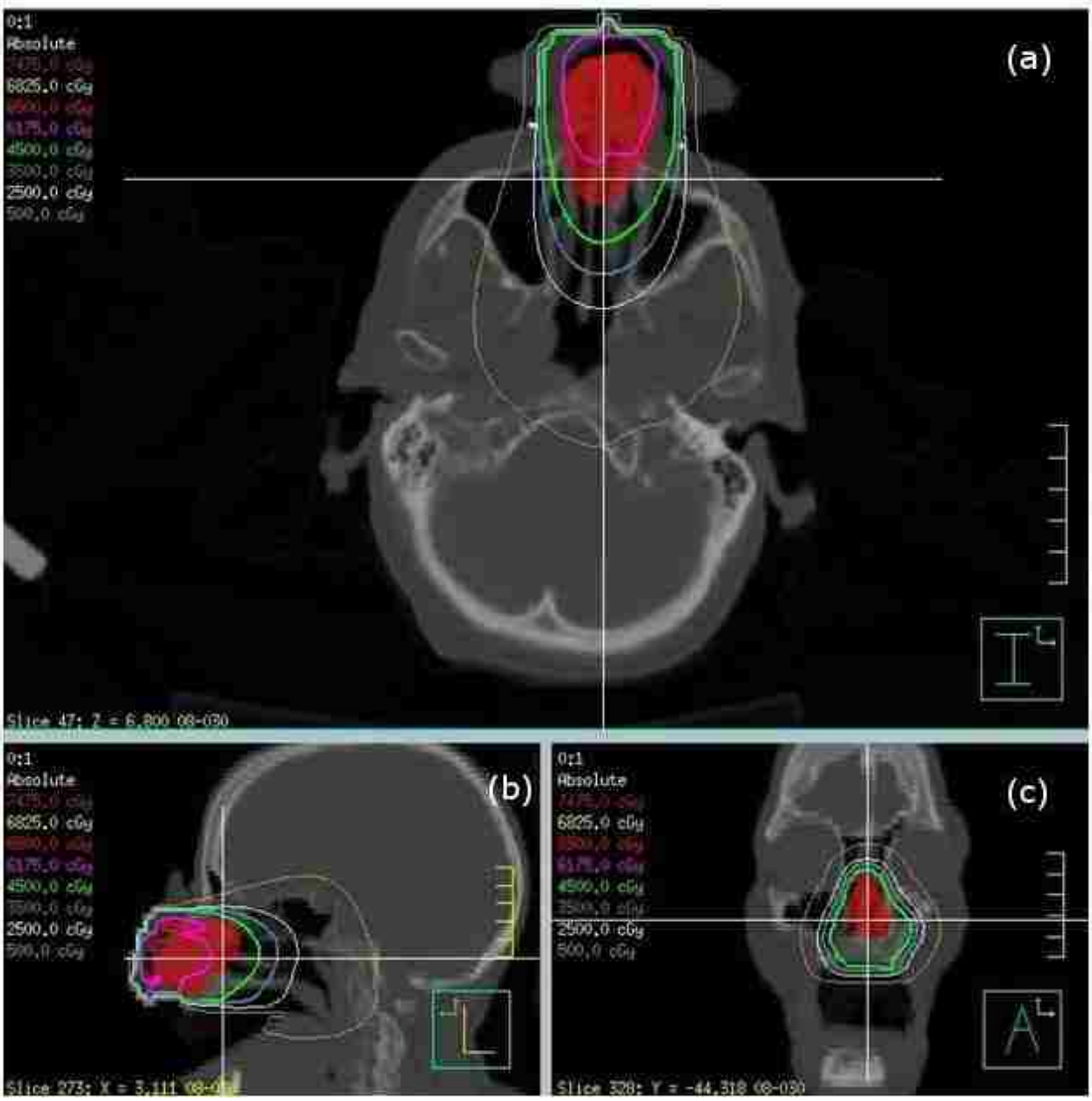

Figure 70 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 0:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

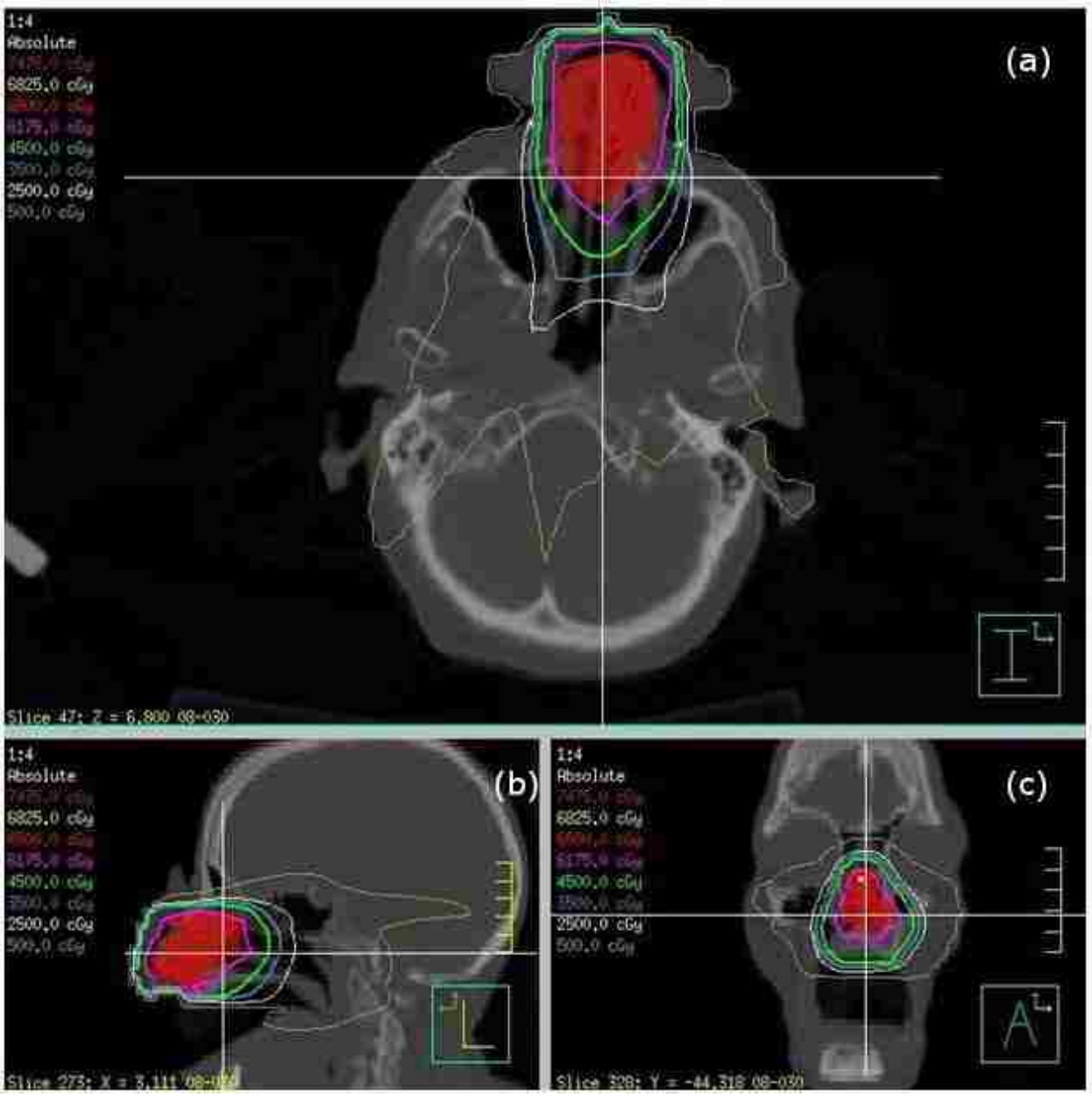

Figure 71 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 1:4 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

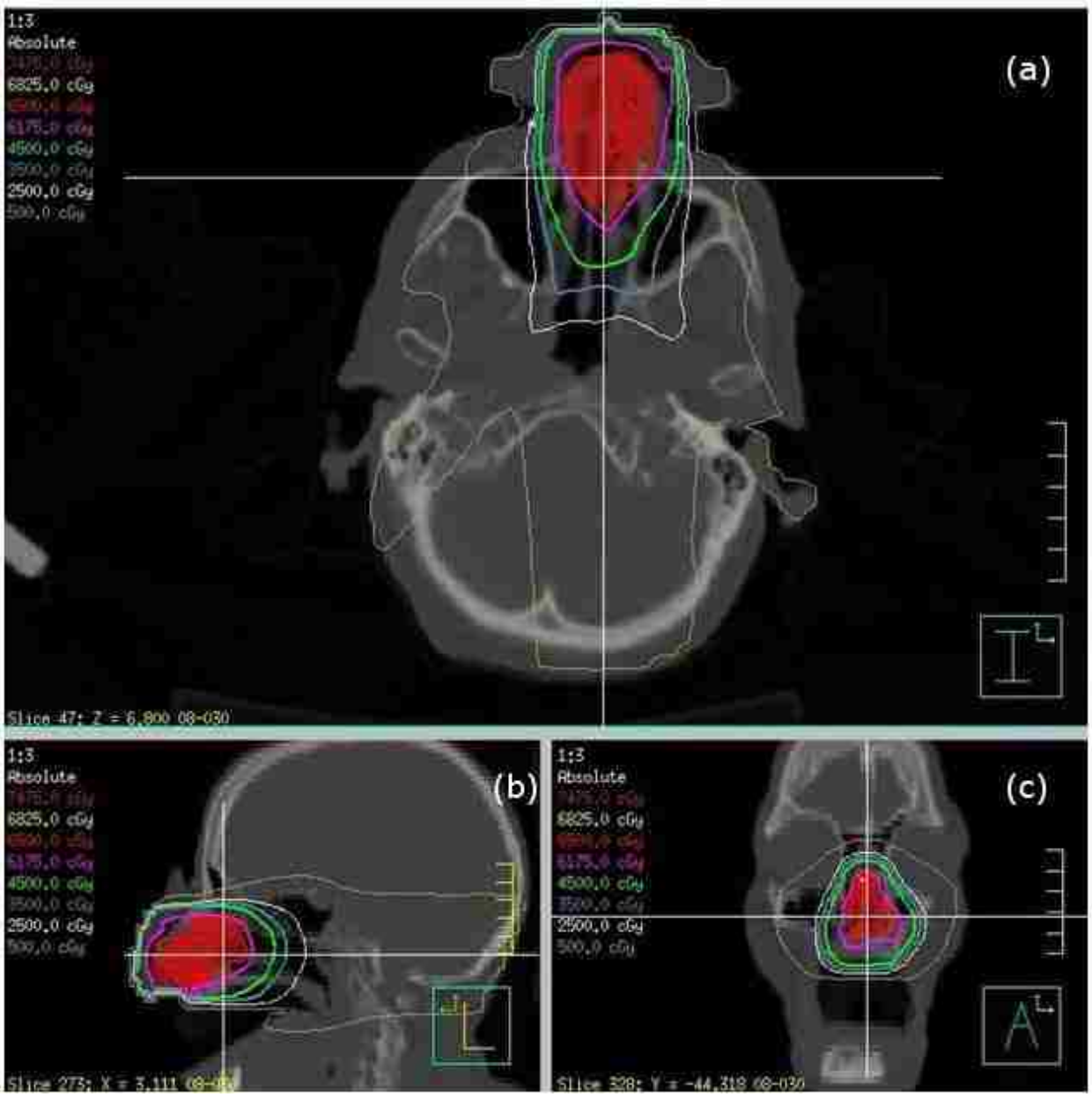

Figure 72 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 1:3 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

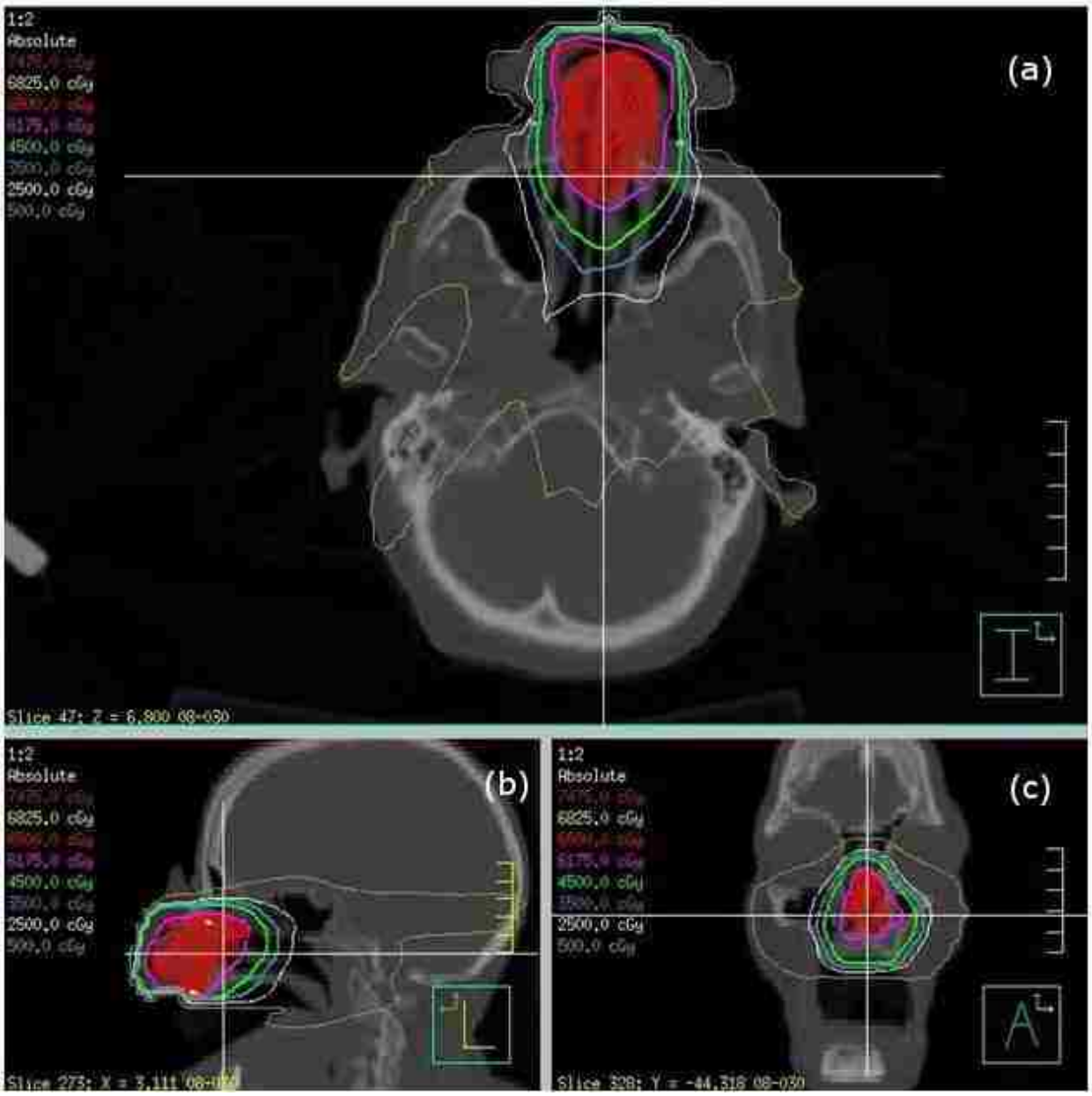

Figure 73 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 1:2 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

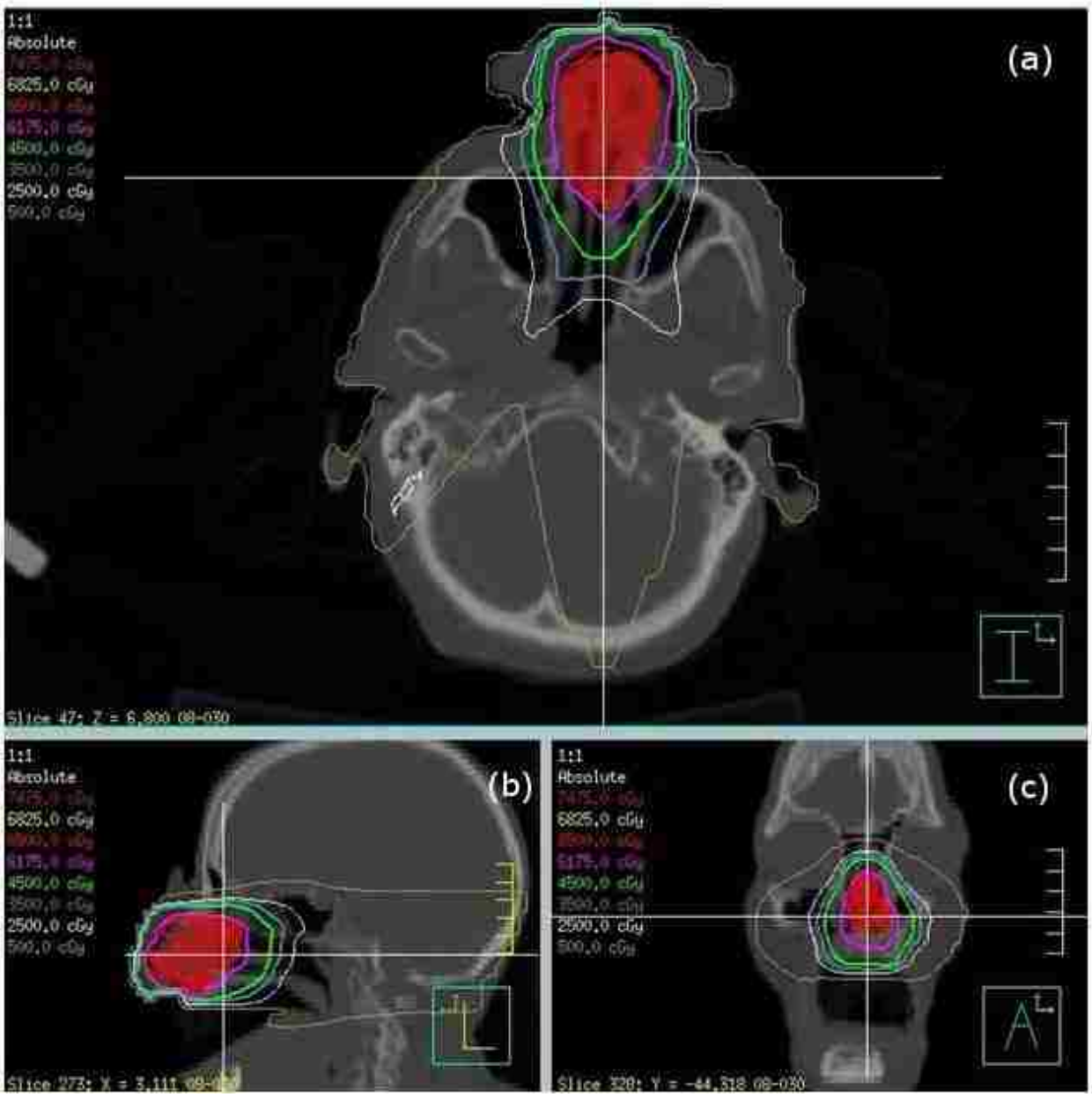

Figure 74 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 1:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

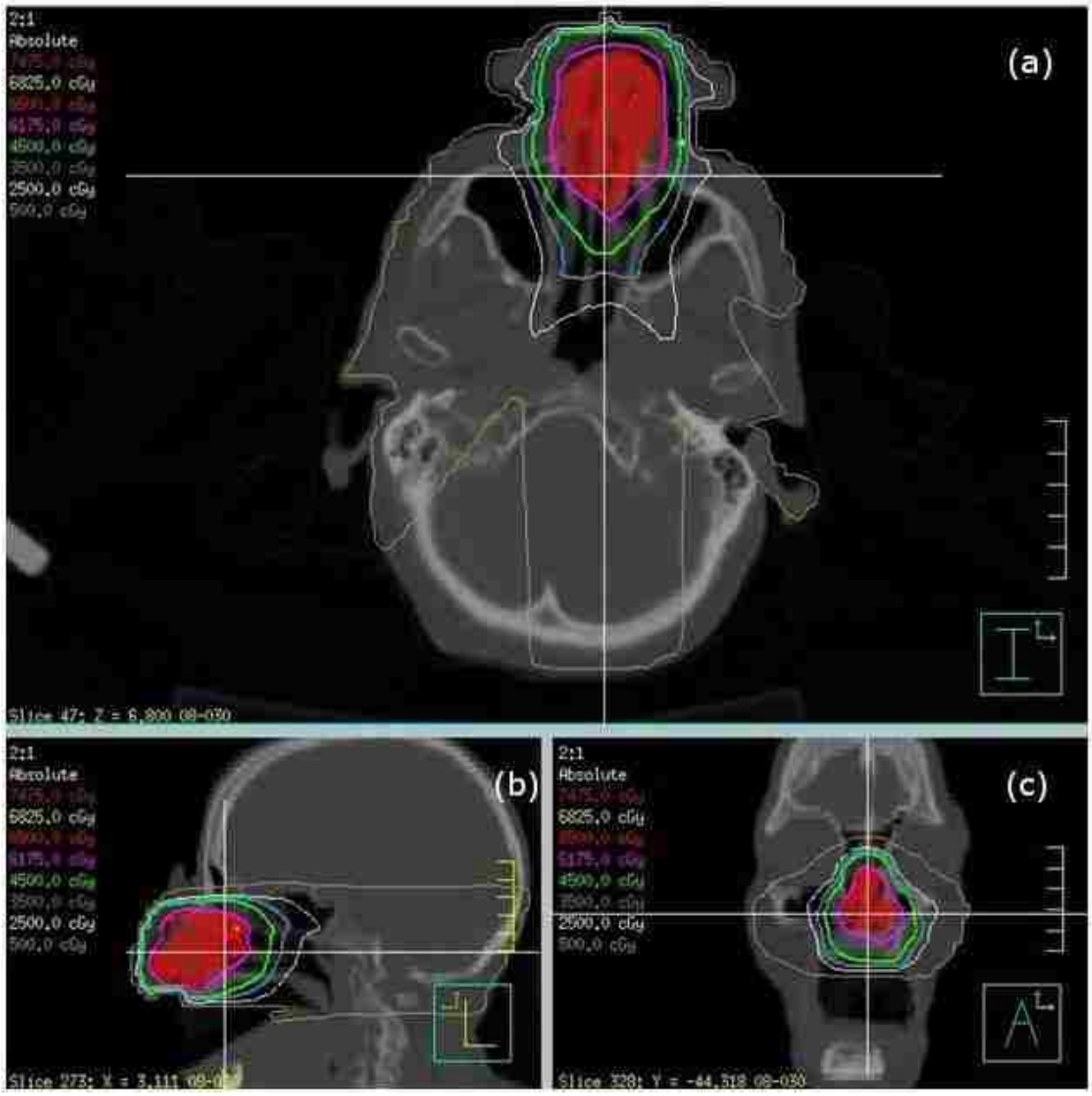

Figure 75 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for 2:1 ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

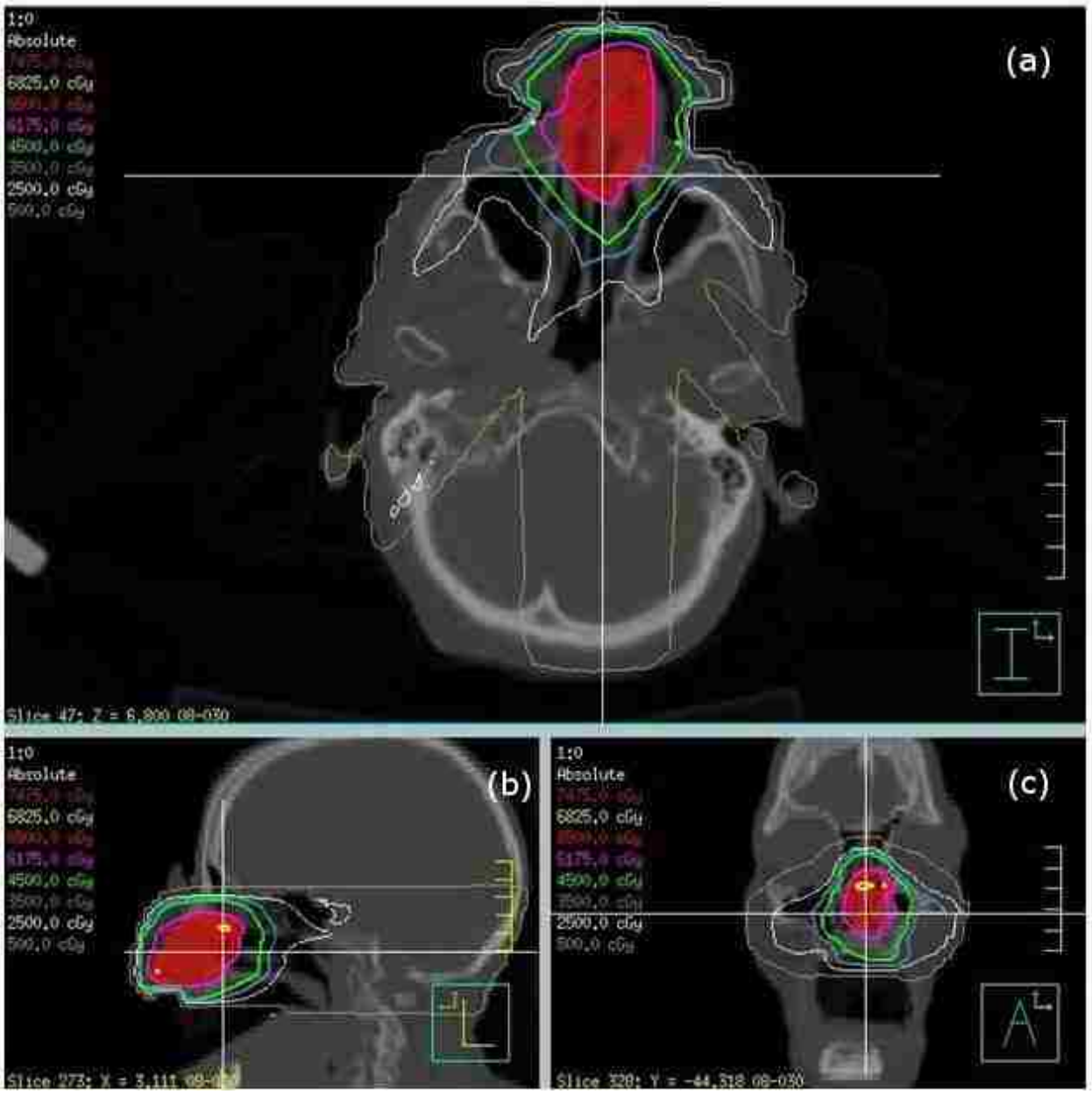

Figure 76 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for the IMRT plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

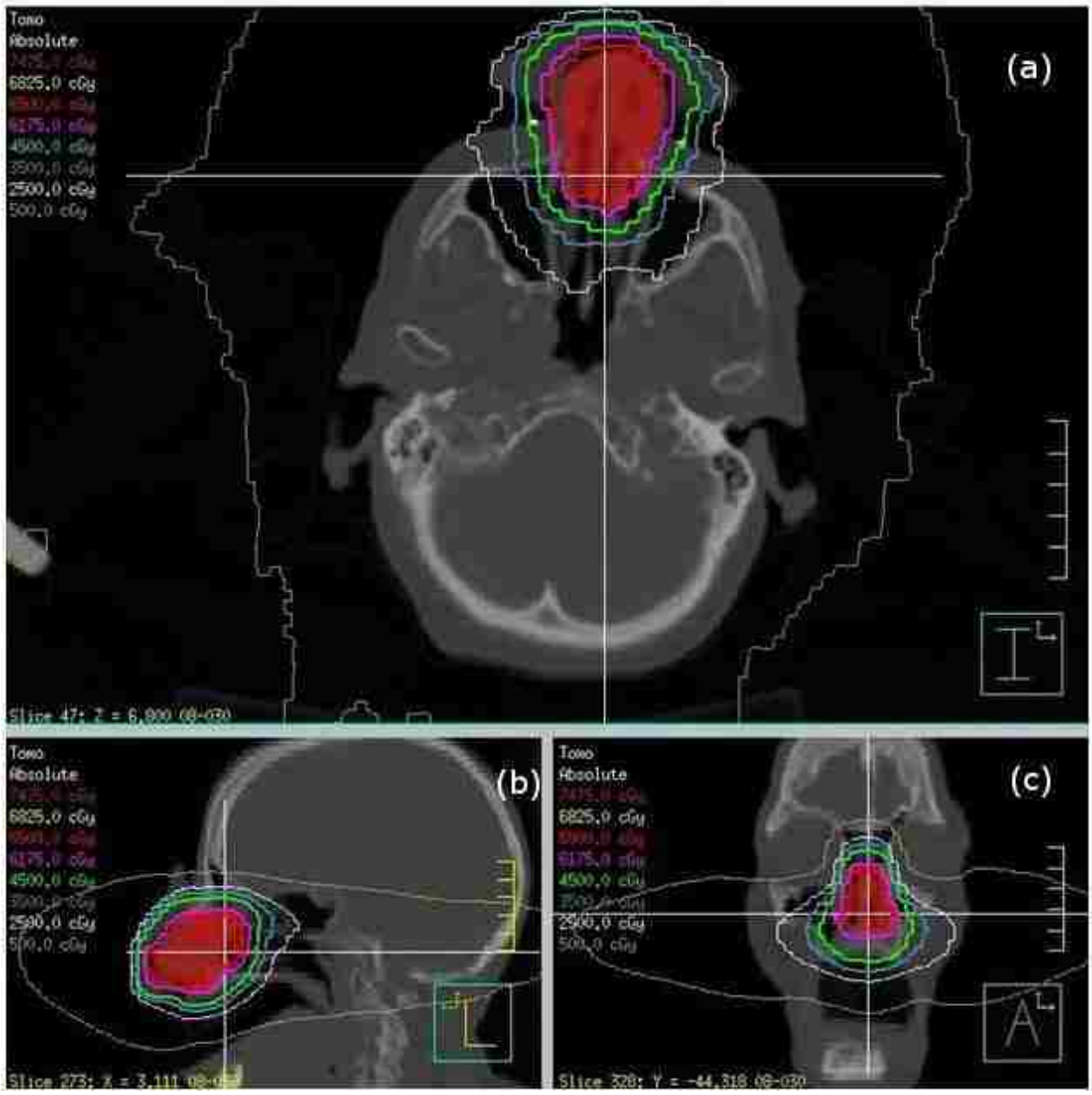

Figure 77 Isodose dose distributions in transverse (a), sagittal (b), and coronal planes (c) through the center of the PTV in patient 5 for the TomoTherapy ratio plan. The white crosshair indicates the position of the planes shown. The PTV is displayed as red colorwash

Vita

Olivier Blasi was born in Trinidad, Colorado in 1983. He is the oldest son of Donald and Christiane Blasi and has one brother and one sister. He began his education at Alliance High School in Nebraska. After graduation from high school, he went on to the University of Wyoming in Laramie, Wyoming to pursue a degree in physics and mathematics. Upon graduation from the University of Wyoming in 2006, he began his master's work at Louisiana State University. He is now a candidate for the degree of Master of Science in the Department of Medical Physics.