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Robust Treatment Planning Concepts and Optimisation for scanned proton therapy

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Abstract

Background

Current margin concepts in proton therapy are adapted from photon therapy and use the extension of the clinical target volume (CTV) to the planned target volume (PTV) to account for setup and range uncertainties. The feasibility of alternative margin concepts, in particular robust optimization, which does not use the extension to the PTV, has been investigated.

Methods and Materials

This study included eight ependymoma patients, whose data has been provided by the Paul-Scherrer Institute in Switzerland. The patients were originally treated with a prescription dose D_{pr}=59.4 Gy(RBE) in 4 series. The plans were recreated using the treatment planning system RayStation 4.8.102. The margin concepts investigated were the clinically applied margin of 5mm, 2mm margins, beam-specific margins, robust optimization to the CTV and robust optimization to both CTV and organs at risk. Robust evaluation took into account the fluctuation of various dose-volume parameters under the influence of isocenter shifts and range errors. Calculation of the perturbed scenarios, summation of the individual series and extraction of the dose-volume parameters such as the near minimum dose, near maximum dose and mean dose, was performed with the help of a Python script specifically developed for this purpose.

Results

The robust evaluation script performed satisfactory and has been adapted into a generalized form to serve as tool for future use. CTV_{D50}=30.6 Gy(RBE) within a 1% margin, CTV_{D2}<107% of D_{pr} and CTV_{D98}>95% of D_{pr} were achieved for all margin concepts in the nominal scenarios as well as the summed plans. Due to the lack of additional margin meant for symmetrical bone irradiation, the robust plans show slightly lower dose values and higher fluctuation range for some cases in series 1. In the other series, they achieve a similar or better robustness compared

to the 5mm plan, while 2mm and BS margins show higher fluctuation. D_{mean} of the brainstem and $D_{2\%}$ as well as $D_{98\%}$ can be lowered by 4-7% (Series 1-3), 20-30% and 17-24% (Series 1-4) when using robust optimization. Other margin concepts also led to lower OAR values than the RSL plans. Shifts in cranio-caudal and anterior-posterior directions consistently caused the highest deviations from the nominal plan.

Conclusion

Target coverage was acceptable in the nominal case for all margin concepts. 2mm and BS plans show higher fluctuations than the 5mm plan. The dose to selected OARs can be reduced by any alternative margin concept. Robust optimization was particularly beneficial for OARs not in close proximity to the tumor and lowered the overall dose to the patient body by over 1 Gy (RBE).

Contents

1. Introduction

Radiotherapy makes use of the ionizing effect of radiation above a certain energy threshold. Radiation carrying enough energy has the capability of removing bound electrons from the atoms or molecules, leading to their ionization [1]. The value above which radiation is classified as ionizing is usually defined at either 12 eV, which roughly corresponds to the ionization values of oxygen and hydrogen, or at 33 eV, which is the ionization energy for a typical water molecule. The aim of radiotherapy is to damage the atoms that make up the DNA structure of the tumor cells. Depending on the type of radiation, the damage is induced to various degrees by direct and indirect ionization. In the case of direct ionization, the radiation causes the ionization through interaction with the atom or molecule itself. Usually, this happens through the electromagnetic interaction between the charged radiation with enough kinetic energy and the atomic electrons. If the ionization is not the result of direct interaction between the electron and the primary radiation, the process is called indirect ionization. An example for indirectly ionizing radiation would be neutron radiation, which carries no charge. The ionization takes place through secondary particles, such as electrons that result from neutron capture and following beta-minus decay. Photons are capable of directly ionizing matter through the photoelectric effect and the Compton effect, but the vast majority of ionization processes happen through secondary electrons. As such, photon radiation is generally classified as indirectly ionizing radiation. As protons and heavy ions possess electric charge, they interact directly with the atomic electrons and are therefore classified as directly ionizing radiation.

1.1. History of radiotherapy

The discovery of X-rays by Wilhelm Conrad Röntgen in 1895 came at a time where medicine was in need of new techniques to treat certain malignant or benign diseases. In the first months of 1896, the newly discovered X-rays were already used to treat skin lesions [2]. After Röntgen's discovery [3], Becquerel followed

with a report on radioactivity in 1896 [4] while the Curies discovered radium in 1898 [5]. Becquerel and Pierre Curie later worked together to publish a report on the physiological effects of radium in 1901 [6]. Such work gave birth to the idea of using radioactivity to treat diseases and can be seen as paving the way for radiotherapy. Due to the dire need of options, X-rays were used for treatment without deeper understanding of the underlying effects. This led to poor outcomes, necessitating further research to improve treatment [7]. In their efforts to explore radiation, physicists worked towards a better understanding of the atomic model, eventually leading to the use of particle beams as radiation source half a century later. Particularly noteworthy are the works of Ernest Rutherford, who explained radioactivity as the disintegration of atoms and performed experiments that helped to determine the structure of an atom [8]. A breakthrough on the biological front was made by Regaud and Coutard, who studied alternative ways of delivering the radiation dose [9]. Their results showed that fractionated dose delivery could control cancer while avoiding some of the severe side effects [10]. This established the difference between normal and malignant cells in their reaction to the radiation, leading to fractionation being employed until this day.

Along with the understanding of the underlying mechanics of radiation and its effect on the human body, the sophistication of the machines to produce the irradiation also increased. A more powerful X-ray tube developed by Coolidge allowed physicians to treat deeper tumors [11]. It also laid the foundation for the linear accelerator, developed by Widerøe in 1927 [12]. In turn, his work inspired the invention of the cyclotron by Lawrence and Livingstone [13]. With the development of the Betatron, electron therapy started to be used as a treatment option [14]. The need for higher energy particle beams led to the development of the Synchrotron around 1944-1945, which nowadays became the standard for the acceleration of heavier particles to high energy levels [15].

The development of cobalt teletherapy units and the design of linear accelerators working in the megavoltage range allowed for higher penetration depth of their respective radiation [16]. To overcome the disadvantages of the common radiation sources that suffered from wide lateral scatter and passed through the target, treatment techniques using multiple radiation fields were developed. Radiotherapy started to see even relatively more advanced treatment methods as their efficacy could be demonstrated in studies, continuously undergoing further development.

In 1946, Robert R. Wilson was the first one to propose the usage of protons for medical purposes, claiming to be inspired by the medical work of Lawrence and Stone in Berkeley [17]. There the first clinical usage of proton beams took place in

1954, followed by a period of investigation. Proton therapy saw a surge of interest, eventually leading to the development of the first hospital-based proton treatment facility in the 1970's at the Loma Linda University Medical Center [18].

Following protons, heavy ions were also considered as a treatment option. Helium ions were investigated at Berkeley and also saw a limited amount of use for treatment [19]. Pi-mesons and pions were thought to have characteristics suitable for treatment, but the expected results did not appear [20] [21]. Carbon ions were first used at the National Institute of Radiological Sciences (NIRS) in Japan and remain the most common heavy ion to date [22].

1.2. Photon therapy

Radiotherapy as a whole profited greatly from the invention and introduction of computers, which allowed the calculation of dose distributions based on anatomical images. Further technological advances in form of high quality medical imaging made more detailed differentiation between tumor and healthy tissue possible. The development of newer treatment techniques followed, such as conformal radiation therapy (CRT), where the beams can be delivered from several directions and are aligned to the shape of the tumor. Multileaf collimators (MLCs), devices consisting of many leaves which move independantly, allow for such an alignment. Compared to earlier treatment techniques, this reduced the relative toxicity of radiation to the healthy tissue and therefore allowed for higher doses to be delivered to the tumor. However, CRT is based on forward planning and irradiates large parts of the body which are in the beam path.

Intensity-modulated radiation therapy (IMRT) was the next step in the development of photon treatment techniques, allowing for more exact shaping of the beam. It was first described in 1978 [23] and is an inverse planning method based on the modulation of the radiation beam's intensity (fluence). Sophisticated treatment techniques as IMRT, which became standard around the year 2000, made it possible to achieve high accuracy of the dose distribution, making high accuracy in positioning, imaging, delineation and calculation necessary. Thus, approaches including additional imaging during the course of treatment started, called image-guided radiotherapy (IMGT).

More recently, advanced arc-based or rotational therapies were developed to overcome certain limitations of fixed-field IMRT. They are based on the delivery of

the radiation from a continuous rotation of the radiation source and allow the patient to be treated from a 360° angular range called arc. In tomotherapy, the patient is moved through the machine while the radiation is delivered by slit beams. Intensity-modulated arc-therapy (IMAT) was first described by Yu in 1995 [24] as an alternative. A more modern form of arc-based therapy is volumetric modulated arc therapy (VMAT) [25], which varies the rotation speed, shape and fluence output rate of the beam.

1.3. Proton Therapy

The primary goal of any radiotherapeutic treatment is to deliver a homogeneous dose to the target volume while sparing the healthy tissue. Photons are most commonly used for external radiotherapy, but proton and heavy ion beam therapy have seen a surge in usage in the last years, with an increasing amount of corresponding facilities being built [26]. As of the beginning of 2015, over 137 000 patients have been treated with particle therapy since 1954, the vast majority of them with protons [27].

The main advantage of proton therapy lies in its dose profile, as protons deliver most of their energy at the end of their range. The resulting maximum is called the Bragg peak. This dose profile allows for a more precise irradiation of the tumor and potentially reduces the probability of side effects, as the healthy tissue receives less dose than with conventional radiotherapy. Due to the sharp dose fall-off after the Bragg peak, tissue behind the treated tumor volume receives a negligible amount of dose [28]. While heavy ion beams, such as Carbon-ions, share many characteristics including the Bragg peak, their dose profile includes a significant dose tail after the peak due to fragmentation [29].

Proton therapy is mainly used for patients where conventional radiotherapy might not be able to guarantee the proper sparing of healthy tissue. It has a particularly important role in pediatrics, i.e. the treatment of children, as they profit the most from receiving a lower dose outside the main treatment volume [30][31]. One aspect of that is the lowered chance of developing secondary malignancies, which usually occur several decades after the initial treatment. Thus, lowering their probability is particularly important for the treatment of children. Another common application of proton therapy is the treatment of certain types of brain tumors, such as chordoma, chondrosarcoma or in children ependymoma. The close proximity of important organs to those tumors makes the high precision of dose

delivery necessary or at least significantly advantageous. Likewise, using proton therapy for the treatment of ocular tumors leads to a lower probability of unwanted side effects. Ocular tumors are the oldest indication for proton therapy, and can be seen as special case because it requires only low energy protons of roughly 70 MeV. Therefore, some facilities exist that offer only proton therapy for such cancers [26].

The increased precision in dose deposition is the biggest advantage of proton therapy, but also makes it more susceptible to any kind of planning or positioning inaccuracies. One way to deal with those inaccuracies is to add a margin to the clinical target volume (CTV), a concept taken from photon therapy. Doing so results in the planned target volume (PTV), which is supposed to account for the uncertainties and ensure the proper irradiation of the CTV [32]. In practice, this approach has become the clinical standard for photon therapy and was adapted for proton therapy. The obvious side effect of this method is that the additional treatment volume results in additional dose to the healthy tissue, potentially complicating the desired OAR sparing.

One of the alternative concepts to the PTV is robust optimization, an optimization algorithm specifically developed for proton therapy. Rather than using the classical idea of a PTV to account for errors, the robust optimization algorithm instead calculates the worst case scenario under a given range for isocenter shift and density perturbation. It then uses the minimax function to optimize by trying to fulfill the robust optimization objectives as well as possible in the worst case scenario. By design, robust optimization is therefore supposed to yield similar target coverage under the influence of errors with less dose given to healthy tissue [33].

1.4. Imaging in radiotherapy

Size and location of a tumor have to be determined as exactly as possible. As such, any sort of treatment planning relies on medical imaging to provide the anatomical and functional information needed. The most common imaging method used for radiotherapy is X-ray computed tomography (X-ray CT), although other methods such as magnetic resonance imaging (MRI) and positron emission tomography (PET) have their applications as well. CT is used as anatomical imaging modalities and therefore provide information about tumor size, location, morphology and changes to nearby tissue. On the other hand, PET is a functional imaging modality and used to gain insight into the biological functions of the tumor. MRI can be used both for anatomical and functional purposes [34]. A comparison of those

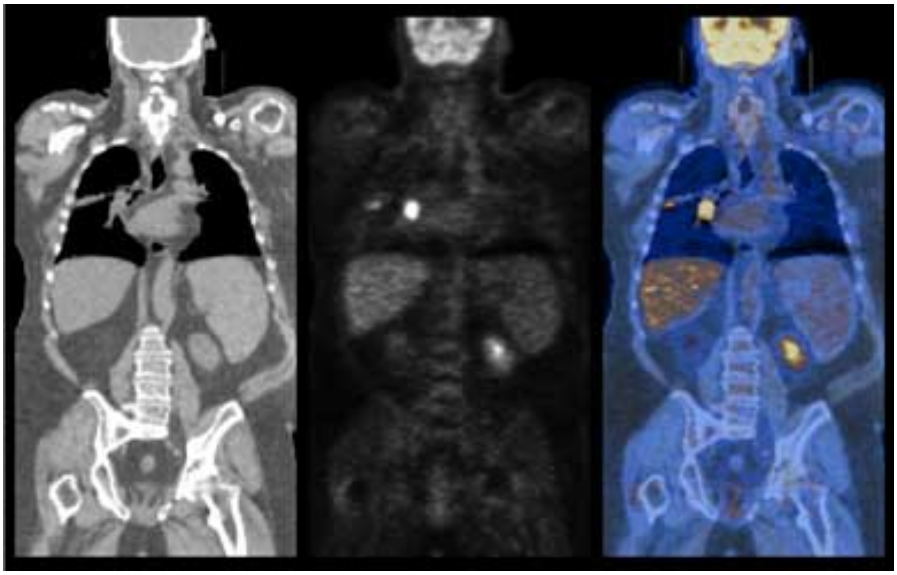

Figure 1.1.: Comparison between CT (left), MRI (middle) and PET (right). http://mis.eng.miami.edu/pet/overview.html; 29.2.2016.

three imaging modalities can be see in figure 1.1.

Computed tomography

Although there are technically other forms of computer tomography, X-ray computed tomography is by far the most common. As such, the term computer tomography usually refers exclusively to X-ray computed tomography. X-rays can be used to create a two-dimensional projection of a volume, as some of the photons are absorbed by the material and not all pass through. The photons which passed through the material are captured by a detector, which provides the two-dimensional representation of the volume. CT is the computer processed reconstruction of the three-dimensional volume structure by combining many X-ray images which are taken from different angles. This is achieved by having the X-ray source rotate around the object, e.g. the patient, while the detectors are placed opposite of the source. In the oldest CT machines the object would have to be moved after every full rotation of the X-ray source, while the later developed spiral or helical CT machines maintain continuous object movement and source rotation. Multi-slice CT machines use several detector rows instead of just one to capture multiple cross-section at once, thereby reducing the scanning time and

slice thickness. Using a very large number of detector rows results in the beam taking the shape of a cone (or technically, a pyramid) and is specifically referred to as Cone beam CT (CBCT) [35].

The initial data undergoes tomographical reconstruction by certain algorithms, such as the well-established filtered back projection or more recently developed iterative techniques. In the images obtained by CT, the relevant information displayed is the relative radiodensity of the scanned material. The radiodensity is quantified with the Hounsfield scale, which is a transformation of the originally measured linear attenuation coefficient. On the Hounsfield scale, distilled water at standard temperature and pressure is defined as 0 Housfield-units (HU), while air under same conditions has -1000 HU. Thus, for a volume elemental with the measured average linear attenuation coefficient μ, the transformation is given as follows.

$$HU = 1000 \frac{\mu - \mu_{water}}{\mu_{water} - \mu_{air}} \tag{1.1}$$

μ_{water} and μ_{air} are the linear attenuation coefficients of water and air, respectively.

Through the use of HU to electron density (ED) calibration curves, which were made on the basis of water phantoms, the HU number gives information about the electron density of the tissue. For proton and heavy ion beam therapy, the electron density has to be converted into the respective stopping power. This information allows for the calculation of the attenuation of the beam, which is a prerequisite for treatment planning [36].

While CT is widely used even outside of radiotherapy due to the achievable resolution and contrast, it comes with the disadvantage of delivering doses up to 0.05 Gy(RBE) to the patient. This is exacerbated in cases where the patient has to undergo multiple CT scans. Thus, it has been considered to account for the dose resulting from the CT scans in radiotherapy [37].

Magnetic resonance imaging

Nuclear magnetic resonance imaging makes use of the fact that hydrogen nuclei possess a spin and therefore a magnetic moment. When an external magnetic field is applied, those protons experience a torque which tries to align the direction of

the magnetic moment with the direction of the external field. As a result, the spin of the nucleus precesses around the direction of the external field with a frequency depending on the field strength. Through the use of a radiofrequency pulse which resonates with the precession frequency and is applied transversally to the static field, the magnetization is also tilted into transversal direction. After the secondary field is turned off again, the spins align with the primary field in their characteristic relaxation time while releasing the energy they absorbed from the pulse. The relaxation time depends on the chemical combination and molecular makeup, leading to different values for different tissue types. This ultimately leads to the necessary contrast in the image [38]. Depending on the magnetic field gradients and radiofrequency pulses used, different tissue types such as fat or fluids can be enhanced or suppressed in the resulting image. Moreover, MRI can also be used to attain functional information [39]. For the purposes of radiotherapy, the advantage of MRI scans lies in its superior soft-tissue contrast, which can be used for organ delineation. However, unlike CT, the MRI scan carries no information about electron density and beam attenuation. As no ionization radiation is used when performing a MRI scan, no additional dose is delivered to the patient. However, the magnetic field interferes with the function of electric devices such as cardiac pacemakers and might not be safe for use with certain implants.

Positron emission tomography

Positron emission tomography is an imaging method where the image is created by tracking the distribution of a radioactive substance which is introduced into the organism. The administered radionuclide (tracer) emits positrons as it decays, which are annihilated as they interact with electrons. The annihilation process creates two photons with the energy of 511 keV and opposing directions. Detectors placed in the form around the patient register those photons, and from them the distribution of the radionuclide within the body can be determined. Unlike CT or MRI, PET doesn't yield morphological data, but only information about metabolic processes within the body [40].

The most common tracer in use is fluoride-18 (F-18) fluorodeoxyglucose (FDG). F-18 FDG is absorbed by cells analogous to glucose, but not depleted as the oxygen atom replaced by F-18 is needed for glucose metabolism in cells. As tumor tissue generally needs more glucose than normal tissue due to their heightened activity, radioactive substance is deposited at a higher rate. As such, PET can be used in the diagnosis or to monitor treatment of certain types of cancer. Examples for other tracers are F-18 fluoromisonidazole and F-18 fluoroerythronitroimidazole,

which are used to image tumor hypoxia [41].

A PET scanner and a CT scanner can be combined into a single gantry so that the images can be taken in the same session and combined into a fused image. Positron emission tomography-computed tomography (PET/CT) therefore makes it possible to align the functional information gained from the PET and the anatomical information from the CT more accurately [42].

Image Registration

As the information about tumor and surrounding organs has to be as exact as possible to allow for accurate delineation of the ROIs, modern treatment planning systems provide the tools for image registration. This allows for the combination of multiple medical images to increase image fidelity, for instance if CT and MRI are used in a complementary manner. At its core, image registration is the transformation of the images into a common coordinate system through a transformation algorithm. There are two overall types of transformation, as they can be either rigid or deformable. In rigid transformations, the distances between any two points is preserved. Therefore rigid transformations are limited to translation, rotation, reflection and any combination of those operations. As opposed to rigid transformations, deformable transformations do not necessitate the preservation of distances.

1.5. Volume concepts

In radiotherapy, the primary goal is to achieve high rates of local tumor control caused by continuous cell death while sparing the surrounding tissue as much as possible. To achieve that it is necessary to delineate all relevant volumes, in order to include them in the treatment planning process. Radiotherapy knows several types of volume concepts to be considered in overall treatment. The ICRU reports 50 and 62 [32] provide the concepts for conventional radiotherapy treatment and the ICRU report 83 [43] further builds on that basis for IMRT. In ICRU report 78, similar methods have been recommended for protons [44]. Figure 1.2 shows the volume concepts that have been outlined in ICRU report 50.

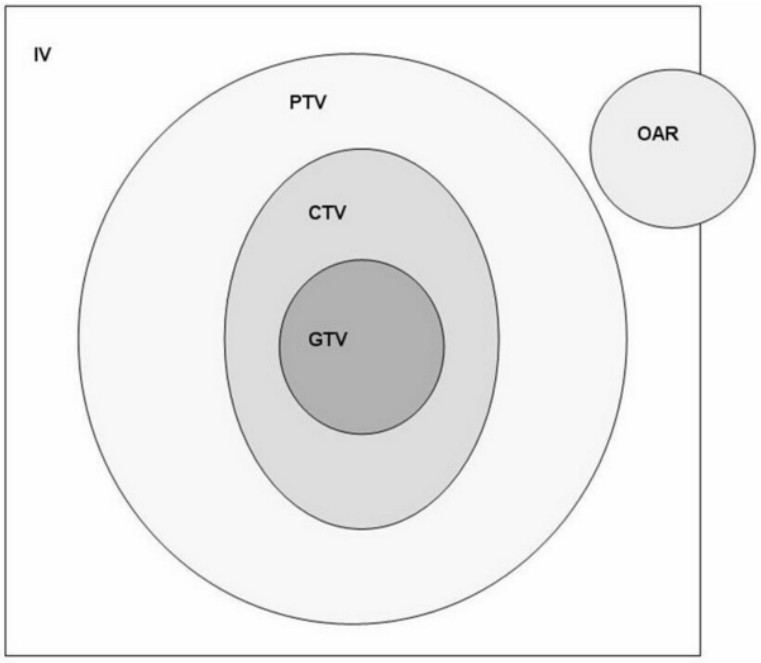

Figure 1.2.: Various treatment volumes used in radiotherapy [32].

Gross tumor volume (GTV)

The gross tumor volume is defined as the spread of the tumor that is directly visible in the image provided by the chosen imaging modality. The GTV consists of the primary tumor as well as possible local or distant metastasis.

Clinical tumor volume (CTV)

As it cannot be assumed that medical imaging is capable of displaying the full extent of the tumor spread, the concept of the clinical tumor volume is introduced. The CTV is usually defined as the GTV plus a certain margin, which should account for the microscopic spread that cannot be seen directly from the image.

Planning target volume (PTV)

Even with increasingly advanced treatment techniques, flawless delivery of the prescribed dose cannot be guaranteed. Due to uncertainties originating from various points such as image artifacts, patient movement, patient positioning, the delivery unit or the treatment planning process itself, the actually delivered dose distribution will differ slightly from the calculated dose distribution. To account for those uncertainties, the CTV is extended to form the planning target volume. The usage of the PTV is meant to ensure that the CTV absorbs the prescribed dose in order to achieve high local tumor control.

Irradiated Volume (IV)

The irradiated volume outlines the tissue that receives a significant dose in relation to the normal tissue tolerance.

Organ at Risk (OAR)

The irradiation of the tumor is always limited by the damage done to healthy tissue. Critical organs which might suffer from the absorbed radiation are delineated as organs at risk to be considered in the planning process in order to be spared.

Planning organ at risk volume (PRV)

To ensure the sparing of the OAR, it possible to introduce the PRV. Analogous to the PTV, the OAR is expanded by a margin to form the PRV.

1.6. Treatment planning

For radiation therapy using photons, protons and heavy ions, there is a distinction to be made between two different types of treatment planning approaches, forward planning and inverse planning. When using forward planning, parameters such

as beam arrangements, weights, energies and compensators are defined in the treatment planning system. Based on those the dose distribution is calculated with sophisticated algorithms. If the result does not meet the clinical requirements, the parameters are changed and the new dose distribution is calculated. This process is repeated until an acceptable treatment plan has been developed. Forward planning is used for conformal radiotherapy using photons and also for proton plans with passive scanning (see chapter 2).

The other approach is inverse planning, such as for IMRT and IMPT. In this approach the optimization is performed by specifying weighted optimization objectives for the target volume and organs at risk. The optimization algorithm optimizes the beam parameters (such as the spots to be used) according to those objectives, which are focused on ensuring target coverage and OAR sparing. The optimization is an iterative process which tries to minimize the sum of the function values, which are a measure of how strongly the objectives are violated. Every optimization objective is a cost function with an associated function value, which is zero if the objective is fulfilled. Inverse planning makes the delivery of more complex dose distributions possible. This makes it the preferred option for tumors close to critical organs or in complex shapes, in particular concave-shaped tumors. More details on treatment planning can be found in chapter 3.

2. Basics of proton therapy

2.1. Physical aspects of proton therapy

Proton therapy is based on the interaction between protons and the irradiated tissue. The proton itself is described by the standard model of particle physics, which concerns the electromagnetic, strong and weak nuclear interactions and classifies all known subatomic particles. The standard model distinguishes between bosons and fermions. The former consist of the gauge bosons, which are the force carriers that mediate the fundamental interactions and the Higgs boson, which is used to explain the mass of other particles. Fermions are the particles which constitute matter and follow the Pauli exclusion principle, meaning that two fermions cannot occupy the same quantum state. They are further divided into leptons and quarks, of which there are six each. Additionally, each fermion has a corresponding antiparticle. The six leptons, which are the electron, electron neutrino, muon, muon neutrino, tau and tau neutrino, do not interact via the strong interaction as they carry no color charge. The neutrinos also carry no electric charge and therefore only interact via the weak interaction. On the other hand, the six quarks, which are the up, down, top, bottom, strange and charm quarks, carry both color and electric charge. They cannot be isolated and therefore only be observed as color-neutral composite particles, which are called hadrons. Hadrons consisting of a quark and an antiquark are called mesons while hadrons consisting of three quarks are called baryons.

The proton is the baryon with the lowest mass, formed from 2 up-quarks and 1 down-quark. It carries an electric charge of +e, owing to the respective $+2/3e$ and $-1/3e$ charge of up- and down-quarks. As opposed to the photon, it carries a rest mass which amounts to 938 MeV/c^2 [45].

Moving protons carry kinetic energy. When passing through matter, such as human tissue, they lose energy through interaction, transferring it to the matter they traverse. Radiotherapy aims to use that energy to destroy the malignant cells. An

important physical quantity is the dose deposited in the material. The absorbed dose is defined as the mean energy deposited in a mass element, with the unit Gray [J/kg] [1].

$$D = \frac{d\epsilon}{dm} \tag{2.1}$$

Ultimately, the amount and distribution of the radiation dose within the patient are the parameters that influence the treatment the most. Due to the way the protons interact with matter, the depth-dose distribution when irradiating tissue takes the form of the characteristic Bragg curve. After the dose reaches its maximum at the end of the curve at the so-called Bragg peak, it falls off sharply, with basically no dose behind the target volume (Fig. 2.1). Additionally, their relative large mass ensures that protons experience little lateral side scatter in the tissue, leading to a more focused beam that does not broaden much [28].

Proton beams with different energies can be used to treat the entire tumor, as a single Bragg peak might not be able to cover it. The combination of the proton beams with Bragg peaks at different depths leads to the spread-out Bragg peak (SOBP), which aims to deliver a uniform dose to the tumor (Fig 2.1).

Coulomb scattering

As protons carry charge, they interact with matter through the electromagnetic force. The interaction with the electric field of the nuclei is termed elastic scattering, where the protons do not lose energy and only experience a small change in direction. Interactions with the atomic electrons are generally inelastic, as the proton transfers a part of its energy, thereby removing the electron from the atom and ionizing the target. The change in direction in this process is fairly minor, but the proton will continuously lose energy through multiple scattering events. Coulomb interaction with the outer shell electrons is the dominant interaction in the entrance region (Fig. 2.2). As the proton keeps losing energy, the frequency of ionization increases quadratically. The rate of energy loss through ionization for particles in general, and therefore protons, can be described through the simplified Bethe formula. Assuming that a particle with velocity v, charge Z_p and energy E travels a distance x through a target material with density N and atomic number Z_t, it loses energy according to the following formula:

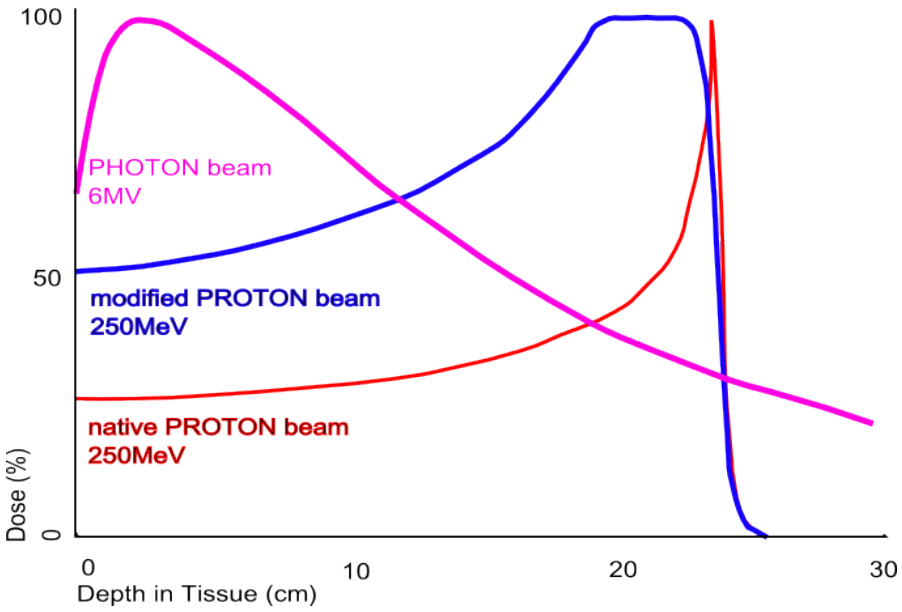

Figure 2.1.: Comparison of the depth dose distribution between photon and proton beams. https://commons.wikimedia.org/wiki/File:BraggPeak.png; 25.2.2016

$$-\frac{dE}{dx} = \frac{4\pi e^4 N Z_t Z_p^2}{m_e v^2} S \tag{2.2}$$

where e and m_e are the electron charge and mass, while S is the stopping function. The width of the peak depends on the variation in energy of the protons, while the height depends on the intensity of the beam. At low velocities, the protons are not only capable of ionizing the target, but can also capture the free electron themselves. That process is also called charge-changing process. As a result, both interactions $p + H_2O \rightarrow H + H_2O+$ and $H + H_2O \rightarrow p + e^- + H_2O$ take place. The interplay of ionization and recombination processes decreases the mean charge state of the protons, so that their charge Z_p has to be replaced with the effective charge Z_{eff}. The effective charge can be described by an empirical formula.

$$Z_{eff} = Z_p[1 - exp(-125\beta Z_p^{-\frac{2}{3}}] \tag{2.3}$$

The relativistic velocity is given as $\beta = v/c$. The maximum rate of energy-loss given by the Bethe-equation is reached at the velocity of

$$v_p = Z_p^{\frac{2}{3}} v_0 \tag{2.4}$$

where $v_0 = \frac{e^2}{\hbar}$ is the Bohr-velocity with the reduced Planck-constant $\hbar$.

The stopping power depends on the material and is generally determined from experiments and simulations. The stopping power is higher in material with a lower atomic number Z. Stopping powers for various materials were presented in the International Commission on Radiation Units and Measurements report 49 [46]. As such, materials with a high atomic number can be used to scatter the protons at larger angles without causing much energy loss, thereby spreading the beam [29].

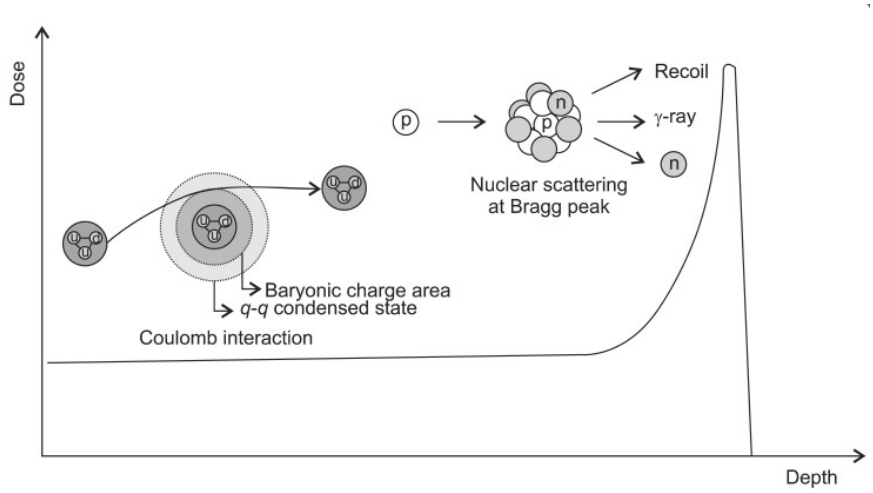

Figure 2.2.: Coulomb scattering and nuclear scattering of protons. [47].

Nuclear scattering

Protons interact with the nuclei of the target material via the strong force. As the strong force is extremely short-ranged, those interactions take the form of collisions. If the interaction is elastic, the proton is scattered by some angle while retaining its identity. Non-elastic scattering however leads to the loss of the primary proton as it reacts with the target nucleus to produce secondary particles, such as secondary protons, deuterons, alpha-particles, neutrons or photons. While the charged secondary particles are mostly absorbed locally, neutrons and photons

have a relatively longer range. Low energy neutrons in particular can produce secondary protons by elastic collision with hydrogen atoms. The overall dose contribution of non-elastic scattering depends on the energy of the proton and is around 5% at 100 MeV, 10% at 150 MeV and 20% at 250 MeV. Around the Bragg peak, where slowed down protons are prevalent, primary protons are responsible for the majority of the dose. Behind the distal edge of the peak, where the range of the initial protons has been mostly exceeded, the absorbed dose is to 70-80% caused by secondary protons which were created by neutron-hydrogen collisions. As opposed to heavy ion therapy, the resulting dose tail behind the Bragg peak is too minor to be a major detriment to the overall treatment [48].

Energy straggling

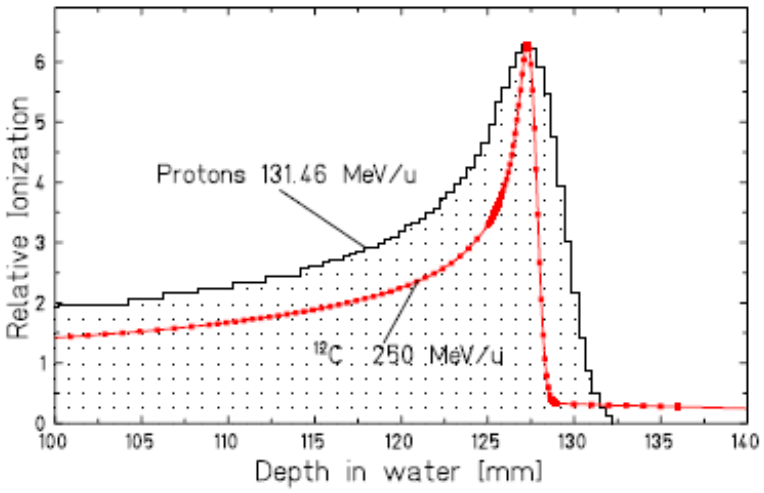

Figure 2.3.: Measured Bragg peaks of proton and carbon ion beams that have the same depth in water [29].

According to the Bethe-formula, the energy loss near the maximum particle range would take the form of an extremely sharp peak for a single proton. In reality, the resulting Bragg peak is broadened due to the primary beam consisting of a multitude of protons (Fig. 2.1). Even with the same initial energy, their actual range slightly varies due to statistical fluctuations of their energy-loss. These fluctuations can be described by the Vavilov-distribution for charged particles passing through a thin layer of matter [49]. Given enough collisions, the Vavilov-distribution becomes a Gaussian function of the following form [50].

$$f(\Delta E) = \frac{1}{2\pi\sigma} exp(\frac{(\Delta E - \bar{\Delta E})^2}{2\sigma^2} \tag{2.5}$$

with

$$\sigma = 4\pi Z_{eff} Z_t e^4 N \Delta x [\frac{1 - \frac{\beta^2}{2}}{1 - \beta^2}] \tag{2.6}$$

The range straggling width σ_R of particles depends on their mean energy and therefore mean range R. Their ratio is nearly constant and can be written as follows.

$$\frac{\sigma_R}{R} = \frac{1}{\sqrt{M}} f(\frac{E}{mc^2}) \tag{2.7}$$

E and M and the energy and mass of the particle, while the function f depends on the target material and only varies slowly. The ratio $\frac{\sigma_R}{R}$ for light ions is around 10^{-3} when absorbed by water, and is smaller for heavier ions due to the mass term (Fig. 2.3). However, the density inhomogeneities occuring in actual tissue lead to their Bragg peaks being broader.

Lateral beam spread

The lateral deflection of particle beams is caused mainly by elastic Coulomb interactions with the target nuclei. Heavy ions are advantageous in comparison to protons in this aspect, as their higher mass leads to a smaller beam spread. The distribution of the scattering angle can be described by an integral equation given by Bothe, with the solution for a shielded Coulomb potential given by Molière [51]. For small angles, the distribution approaches a Gaussian function with the standard deviation given by Highland [52][53].

$$\sigma_\theta[rad] = 14.1 \frac{MeV}{\beta pc} Z_p \sqrt{\frac{d}{L_{rad}}} [\frac{1}{9} log_{10}(\frac{d}{L_{rad}})] \tag{2.8}$$

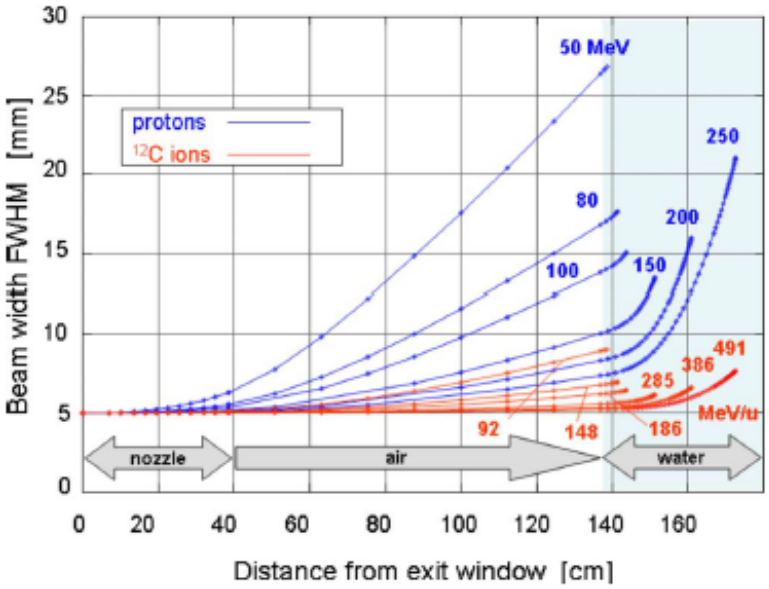

Figure 2.4.: Lateral beam spread calculated for proton and carbon beams of various energies [29].

The target material has the thickness d and radiation length L_{rad}. When comparing proton beams with e.g. carbon ion beams, it can be shown that the spread for protons is more than three times larger (Fig. 2.4). For lower energies, the lateral beam spread is predominantly caused by external material in the beam path. As such, the amount of external material should be minimized. At higher energy levels, the range of the particles rises, which leads to the majority of the beam spread being caused by deflection inside the target material.

2.2. Biological effects of proton beams

All forms of radiotherapy have the goal of damaging the DNA of the tumor cells by means of ionization. Indirect ionization of the DNA atoms is caused by the ionization of water molecules. The thereby formed free radicals, mostly hydroxyl radicals, are responsible for the vast majority of DNA damage in photon therapy. When using protons, the contribution of indirect damage through radicals still outweighs the direct damage by a ratio of roughly 7 to 3 [54].

Relative biological effectiveness

Photon and ion beam radiation do not only have different physical properties such as the depth dose, but also a different biological effectiveness. Depending on the source of radiation and the type of tissue, the same physical dose might lead to different results in terms of tumor control and normal tissue effects. A very common way to quantify those differences is the usage of radiation weighting factors for both radiation and tissue type. Those weighting factors are used in radiation protection, and are designed as upper limits to ensure that the potential impact of radiation on an exposed person is never underestimated. Even though they are loosely based on the biological effectiveness of the particles, they do not accurately represent the actual biological response to particle beams and are therefore not suitable for use in radiation therapy.

Instead, radiotherapy makes use of the concept of the relative biological effectiveness (RBE) to account for the properties relevant for radiotherapy. The RBE is defined as the ratio between the physical dose of a reference radiation and the physical dose of the considered radiation that have the same biological effect. Generally, photon radiation serves as the reference for the relative biological effectiveness of other types of radiation. To account for the effect of the RBE in clinical practice, it is common to speak of the RBE-weighted dose in Gy(RBE) as seen in formula 2.9.[44].

$$RBE = \frac{D_{ref}}{D_{ion}}|_{biologicaleffect=constant} \tag{2.9}$$

For heavier ions like carbon ions, the RBE varies by dose level, radiosensitivity of the irradiated tissue, the energy of the radiation and the fractionation. It can also be defined for different biological endpoints, of which tumor control and normal tissue complications are the most relevant ones. In proton therapy, their comparatively low linear energy transfer allows the definition of a "clinical RBE" at a fixed value 1,1 for the entire radiation field. However, the RBE does vary slightly especially at the distal edge of the Bragg peak, where a significant increase of the RBE could be measured [55]. The intricacies of the RBE become more important for heavy ion therapy, for instance the RBE values for carbon ion radiation range between 3 and 20 [29].

The differing biological effectiveness in general is a result of the damage that the DNA of the irradiated cells experiences. Distinctions can be made between

single strand breaks, double strand breaks and base damage to the DNA. The more complex and localized the DNA damage is, the more likely it is that the repair mechanisms of the cells are insufficient. Double strand breaks in particular are likely to prevent cell division and lead to eventual cell death. In the case of photon radiation, the low cross-sections of the ionization processes necessitates a high number of photons to deliver significant doses. Their ionization density can be seen as homogenous throughout the cell volume, leading to higher average distances between damage locations and a lower probability of double strand breaks. For heavy ions, their high ionization density along the paths of the particles leads to more localized, complex DNA damage [56].

Oxygen enhancement ratio

Apart from their higher RBE, there is another advantage of heavy ions and to a lesser extent protons when dealing with tumors deprived of oxygen. The radiosensitivity of tissue in general depends on its oxygen saturation, with hypoxic conditions being detrimental to the effectiveness of radiotherapy. This effect is described by using the oxygen enhancement ratio (OER).

$$OER = \frac{D_{hypoxic}}{D_{aerobic}} \tag{2.10}$$

$D_{hypoxic}$ and $D_{aerobic}$ respectively are the doses with reduced and normal oxygen supply that lead to the same biological effect. For conventional radiotherapy the OER is around 3, while it is significantly reduced for heavy ions. Ions that are heavier, such as carbon ions, show an even lower minimum OER than lighter ions such as helium [57]. The reason for their high potential in the treatment of hypoxic tumors is the higher radiation damage through direct hits.

2.3. Accelerators for proton beams

In order to perform particle therapy, the particles have to be accelerated to the energy levels necessary to reach the tumor. Depending on the type and location of tumor, the energy for protons ranges up to 250 MeV. To achieve those energy levels, particle accelerators are used. Two types of accelerators were under con-

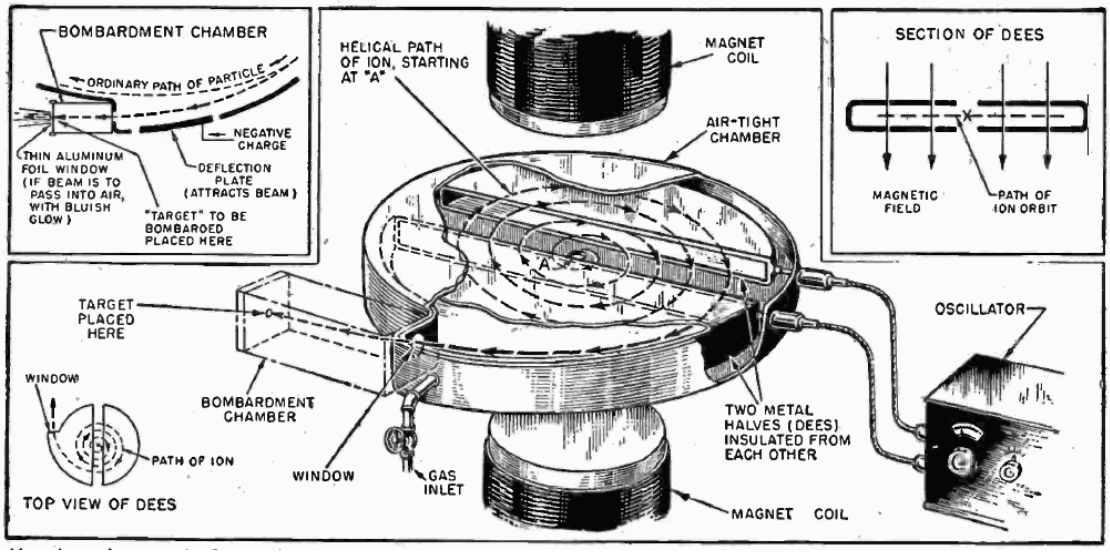

Figure 2.5.: Composition of a cyclotron [59].

sideration to be most appropiate ones for particle therapy, the cyclotron and the synchrotron. Both accelerator types are in use for protons, while heavy ion beam therapy exclusively uses synchotrons [58].

Cyclotron

The composition of a cyclotron can be seen in figure 2.5. Charged particles are accelerated outwards from the center using high frequency alternating voltage while being kept on a spiral path with the use of a static magnetic field. The voltage is applied to two hollow, "D"-shaped metal electrodes called dees, between which the particles move. Due to the external magnetic field applying the Lorentz force, the particles would travel in a circular path without any additional factors. They are accelerated by high frequency radio pulses which match the cyclotron resonance frequency f, which is given by equation 2.11.

$$f = \frac{qB}{2\pi m} \tag{2.11}$$

Where B is the strength of the magnetic field, q the charge and m the mass of the particle. With the frequency set as this, the particles complete one circuit during

the duration of one voltage, after which the polarity of the voltage is reversed. The electric field is therefore always in the direction to accelerate the particles, causing it to travel in circles with an increasingly larger radius, and thus a spiral path [60].

The energy of the particles depends on the radius R of the dees, as it determines the amount of times it experiences acceleration due to the electric field. The maximum energy particles can gain is limited by relativistic concerns, as particles can only be accelerated to velocities much slower than the speed of light. For non-relativistic particles, their output energy is determined by the equation of the centripetal and the Lorentz force.

$$\frac{mv^2}{R} = qvB \tag{2.12}$$

Where v is the velocity of the particle. Therefore, their energy is as follows.

$$E = \frac{mv^2}{2} = \frac{(qRB)^2}{m} \tag{2.13}$$

The main advantages of the cyclotron are the ease of operation and the extremely stable beam intensity they offer. However, as they offer no energy variation, external elements in the beam path in form of range modulators have to be used to achieve lower penetration depth.

Synchrotron

The synchrotron is a cyclic particle accelerator descended from the cyclotron, which was developed to reach higher energies. They are used to accelerate protons and heavy ions as well as positrons and electrons, although the latter require a different design. In a synchrotron, the particles follow a closed path consisting of straight parts, where they are accelerated with high frequency electric fields, and curved parts where they are bent and focused by magnets. Radio frequency cavities are used for direct acceleration, dipole magnets are used as bending magnets to deflect the particles, and quadrupole or sextupole magnets are used for focussing. As the particles are accelerated, the magnetic fields can't be static and have to be adapted to the particles velocity to keep all particles on the same path. Synchrotrons are

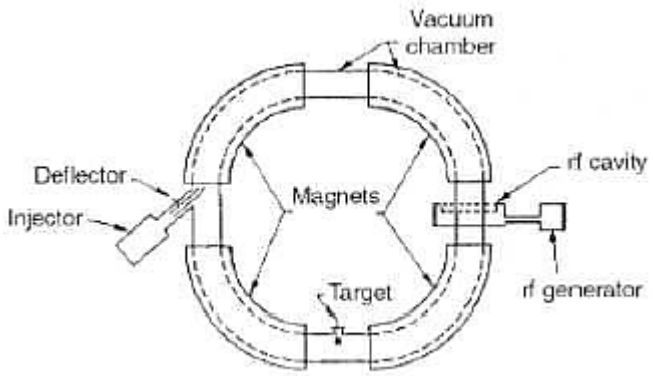

Figure 2.6.: Basic schematic of a Synchotron [60].

unable of accelerating particles from zero energy, and require a pre-accelerator from which the particles can be injected into the ring path [60]. The velocity of protons and heavy ions rises significantly in the synchrotron, and also necessitates the variation of the electric fields used. Therefore electrons and positrons are already injected at nearly the speed of light and only gain energy and impulse as described by relativistic formulas. As such, the technical prerequisites vary significantly and synchrotrons for protons and heavy ions differ from synchrotrons for electrons and positrons. Proton and heavy ion synchotrons operate in pulse mode. Each pulse cycle starts with the injection of the particles, which then experience a period of acceleration. In the period of maximal magnetic excitation, the particles are available for delivery. The extraction of the particle beam is followed by a period of deceleration [61].

The synchrotron allows for variation of the particle beam range by using different acceleration energies, opening possibilities for more optimized treatment. However, they are harder to operate than cyclotrons and require sophisticated injection and extraction systems. Figure 2.6 outlines the basic structure of a synchrotron.

2.4. Beam delivery

The goal of radiotherapy is the proper irradiation of the target volume in order to achieve the best possible rates of local tumor control while sparing the surrounding tissue. In order to do so, it is necessary to shape the radiation beam according

to the tumor spread. Two different techniques of doing so exist for proton and heavy ion beams, passive scattering and active scanning. In passive beam delivery, external elements are used to broaden the beam to make it align with the target volume shape. When using active scanning, the narrow pencil beams are used to irradiate the entire volume by consecutively targeting different spots within the patient [29].

Passive scattering

Passive scattering aims to adapt the beam in three dimensions. The initially narrow beam has to be spread out to cover the target volume, and have its range adjusted accordingly. To achieve the deformation of the beam, a number of external elements such as ridge filters, scattering magnets, range-shifters, collimators and compensators are used (Fig. 2.7). The field aperture is determined by collimators, which adapts the beam to the desired isodose distribution. It cuts out a field corresponding to the tumor contour in beam eye's view and does not let through particles outside the field.

Compensators are beam-shaping elements of varying thickness. They are used modify the depth profile at the distal edge of the tumor and have to take into account not only the tumor shape, but also the complex tissue composition. Commonly, proper tumor coverage is achieved by combining several proton beams with slightly varying energies. By overlapping, the Bragg peaks of the different beams form the spread-out Bragg peak. Range shifters are absorber plates that are used to shift the depth of the SOBP if necessary. While insertion or removal of range shifters is quick, they may broaden the beam. As such, they are placed before the collimator in the passive beam scattering system.

While some of the scattering elements fulfill a general role and can be used regardless of the patient, collimators and compensators have to be individually tailored to the target volume. Another disadvantage of the scattering elements is the loss of radiation and production of secondary particles through their interaction with the initial beam. Secondary neutrons in particular can cause a significant amount of additional dose that might lead to the induction of secondary cancer. The advantages of passive scattering lies in the robustness of the plans, as the lowered complexity compared to active scanning makes it less susceptible to minor uncertainties in beam position or range [62].

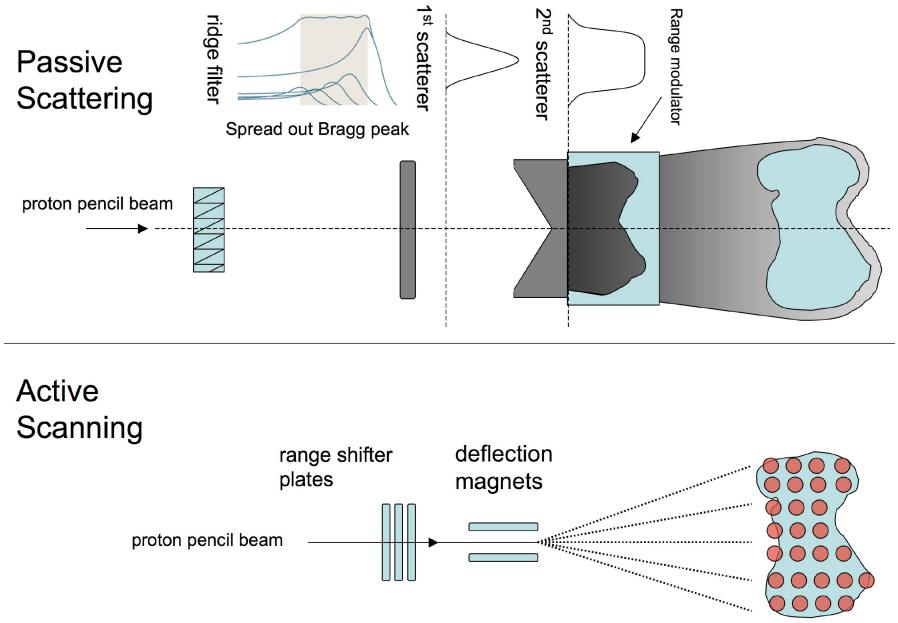

Figure 2.7.: Differences between passive and active scanning systems. [63].

Active scanning

Active scanning aims to deliver the dose using many narrow pencil beams of different energies. In every volume element, the dose results from the superposition of beams which target different spots. Those spots are irradiated sequentially in order to deliver the desired dose to the target volume. In a typical treatment up to several thousand spots in around 40-70 energy layers are used, with their placement and weight determined by the planning system. The control of beam direction necessary for the scanning is provided by magnets. The radiation can be delivered using either raster scanning or discrete spot scanning. In the former case the beam is moved continuously while its energy is varied. When using discrete scanning, the beam is turned off between the spots, corresponding to the pulses in which synchrotrons operate. Active scanning is an inherently intensity-modulating method. Analogous to IMRT, the term intensity modulated particle therapy (IMPT) has been introduced [64].

An advantage of the active scanning method lies in the possibility of dose variation even within one layer of energy, allowing for the delivery of a more complex and exact dose profile. The initial variation in particle energy makes it possible to con-

form the dose distribution to the proximal and distal edges of the target volume. Therefore, the amount of external material in the beam path can be minimized and no patient-specific hardware in form of compensators or collimators is necessary (Fig. 2.7). However, range shifters can still be used to reduce the beam range if necessary. Due to the reduction of external material, the beam losses and the production of secondary neutrons are significantly lower than with passive scattering systems. However, active scanning necessitates strict controls and maintenance of the control and safety systems as well as requiring higher accelerator performance in terms of stability. Due to the inherent modulation of the radiation field, the treatment plans are more susceptible to positioning or range errors in general.

2.5. Treatment techniques

Depending on the optimization strategy, one can distinguish between single-field optimization (SFO) and multi-field optimization (MFO). SFO is based on the independant optimization of all radiation beams. Every single beam is optimized to provide a homogeneous and uniform dose to the target volume. When used in combination with active scanning methods that allow for intensity-modulation, the spots are weighted in a way that achieves that aim. The approach of SFO can be compared to conformal radiotherapy, which uses photon beams with constant fluence. The advantage of SFO plans lies in their inherent robustness due to the individual optimization of the beams. As each radiation field is meant to deliver the same homogeneous, uniform dose to the target, the technique is less susceptible to proton range uncertainties. SFO can be performed both with passive scattering and active scanning systems. A disadvantage of SFO lies in its limitations in regards to organ sparing, which might demand the use of auxiliary help structures.

MFO is based on the simultaneous optimization of all beams including all scanning spots. Therefore, active scanning is a prerequisite for MFO. The optimization of all beams including all scanning spots at the same time allows for the delivery of more complex dose distributions. Compared to SFO, its ability to spare nearby OARs is enhanced. However, due to the concurrent optimization of the Bragg peaks, MFO is more susceptible to uncertainties in proton range [64].

2.6. Uncertainties in proton therapy

Any form of radiotherapy has to account for the existence of uncertainties that can influence the treatment. The goal is the proper coverage of the tumor while sparing healthy tissue. Uncertainties make it harder to adhere to that goal and can lead to the loss of target coverage and normal tissue complications. Compared to conventional radiotherapy, proton therapy is more suspectible to uncertainties because protons have a finite range. That finite range is its biggest advantage as it allows for a more exact dose deposition in the tumor. Therefore the range of the protons has to be predicted as accurately as possible to avoid that the high dose region resulting from the Bragg peak directly shifts into a nearby organ [65].

Uncertainties result from many factors that can lead to a discrepancy between planned and delivered dose. Those inaccuracies have their origins in the patient set-up or motion. Set-up errors include systematic errors related to aspects of the beam delivery system, such as the beam positioning, as well as random errors. Organ motion refers both to changes within a single fraction (intrafraction motion) as well as changes between fractions (interfraction motion). Common examples for intrafraction motion are bowel movements, respiratory movements and the heartbeat, while an example for interfraction motion would be the bladder or rectum filling level influencing the organ position. Positional changes due to organ motion also alter the density in the beam path, leading to additional proton range inaccuracies. When using active scanning methods, intrafraction motion with a frequency similar to the scanning frequency leads to an interplay effect, causing unintentional cold or hot spots in the target.

Another cause for uncertainties lies in the CT scans used (chapter 1.4). The CT scan displays the density of the tissue in HUs, which is converted into the proton stopping power to determine the range. Inaccuracies can arise from either errors in the conversion or errors in the HU values themselves due to image artifacts [66]. Sources for those image artifacts could be metal implants, the scanner being unable to differentiate between a small amount of high density material and a high amount of low density material (partial volume effect), an increase of the mean energy of the scanning beam due to the lower energy photons being absorbed (beam hardening), or simple stochastic noise among others [67]. Uncertainties and their relative influence on the total range uncertainty are shown in figure 2.8.

The proper accounting for the effect of uncertainties is paramount for the success of the radiotherapy treatment. Measures to reduce uncertainties range from additional immobilization of the patient through facial masks to image guidance based

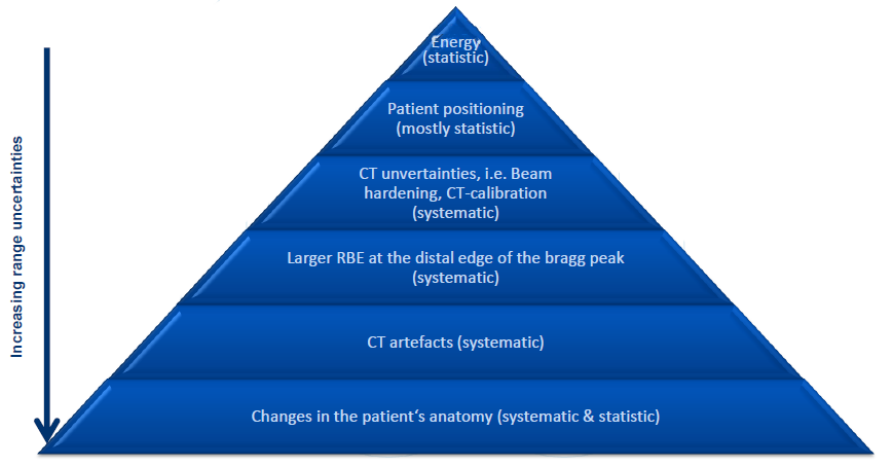

Figure 2.8.: Various statistic and systemic uncertainties in order of relative influence. Figure courtesy of Barbara Knäusl, adapted from Lomax.

on anatomical acquired directly before the treatment fraction. To mitigate the effects of organ motion specifically, several strategies exist.

The simplest of them is the expansion of the target volume to account for both positioning and density errors. Ideally, the PTV should cover the entire area of the moving CTV to ensure the target coverage 1.5. By itself the expansion of the target volume is not sufficient for active scanning methods, as it does not take the interplay effect into consideration. The limitation and main drawback of this method lies the additional dose to healthy tissue that is accrued. An alternative to the PTV is the use of robust optimization, which is a method based on minimizing the effect of the worst case scenario.

3. Treatment planning

3.1. Treatment planning process

In the radiotherapy workflow, treatment planning is the process that design the concept for delivering the prescribed dose as accurately as possible. It is conducted with treatment planning systems (TPS), which calculate the dose distribution in the body of patient. The dose calculation is based on the available anatomical, functional and tissue density information of medical images, most commonly CT. Furthermore, several treatment parameters have to be defined during the treatment planning process, such as the number and directions of the used beams, the dose prescription, fractionation schedule and type of radiation.

3.1.1. Structure definition

For the creation of a treatment plan, certain regions of interest (ROI) have to be delineated on the CT image, a task which is performed by the radiation oncologist with support of the radiotherapy technicians and the medical physicist. The ROIs can be any type of target volume, OARs or miscellaneous ROIs such as external fixation structures. The delineation can be done manually or semi automatically with the help of functions that can recognize structures based on the density differences obtained from the CT scan.

The basic volume concepts used in radiotherapy are described in chapter 1.5. The planning target volume is the general concept used to ensure that the dose will be delivered to all parts of the CTV with an acceptable probability, even when facing uncertainties. Its delineation is sometimes takes additional considerations into account, such as expanding the PTV to ensure symmetrical bone irradiation. In cases where the PTV encroaches or overlaps another PTV, OAR or PRV, ICRU report 83 recommends to adjust the PTV used for optimization based on specfic

tumor circumstances [43]. In practice the PTV margin is usually adapted to avoid overlap with OARs. Alternatively, the PTV can be subdivided into sectors with different prescription doses. However, the delineation of the CTV is never compromised in any circumstance.

The outer body that can be seen in the CT is also a ROI, and required for most TPS. Its main functions are to serve as a basis for the dose calculation grid as it signifies the area for which the dose has to be calculated, and to aid with image registration.

3.1.2. Plan design and evaluation

The treatment plan is created with the primary goal of delivering the prescription dose to the target ROI. The prescription dose value usually refers to the median dose ($D_{50\%}$) in the target ROI, which is typically the PTV [43]. Apart from the prescription, it is also necessary to define the patient position (head first supine or feet first supine), treatment beams, treatment method, the type of radiation used and the fractionation schedule. The patient position usually reflects the position in which the original CT-scan was taken. Different treatment techniques are described in chapter 2.5. When choosing the number of beams and their angles, the technical restrictions of the available beam delivery system have to be considered. Furthermore, they have to be chosen in a way that adhers to the original goal of delivering the dose as accurately as possible while sparing surrounding tissue. While tumors at a relatively low depth might be treatable with a single beam, tumors that are harder to reach often need multiple beams. The beams also have to be chosen with the uncertainties in radiotherapy in mind. In proton therapy, the particle range is one of the most significant sources of uncertainties. By choosing beam paths that cross mostly homogeneous tissue while avoiding areas with higher movement, the range uncertainty can be reduced. Beams along the direction of motion will also suffer from less range uncertainty than beams perpendicular to that motion. Minimizing the impact of those uncertainties enhances the robustness of the plan, ensuring a more accurate delivery of the dose. Moreover, uncertainties have a higher impact if the high dose region is extremely close to an OAR, which is why this scenario should be avoided.

An important part of treatment planning is the assessment of the plan quality. Several metrics to that purpose exist, such as isodose curves and dose-volume histograms (DVH). Isodose curves are lines tracing points of equal dose and are usually expressed as a fraction of the prescription dose. As such, they offer spatial

information regarding the distribution of the radiation dose. DVHs represents the radiation dose as a two-dimensional histogram and therefore does not offer such spatial information. They give an overview of the dose levels experienced by the target volume and OARs. The following dose-volume points on the DVH curves are recommended by the ICRU to use for plan evaluation [43].

- Dose at 2% of the volume ($D_{2\%}$), as a surrogate for the maximum dose
- Dose at 50% of the volume ($D_{50\%}$), the median dose
- Dose at 98% of the volume ($D_{98\%}$), as a surrogate for the minimum dose
- Volume at 95% of the dose ($V_{95\%}$)

In clinical practice, it is important to ensure that healthy tissue, in particular OARs, is spared as much as possible. Different organs have difference tolerance to radiation dose, with the OAR constraint values being obtained from clinical studies and/or experiments, respectively.

3.2. Treatment plan optimization

To avoid unnecessary dose to organs at risk, it is necessary to optimize the treatment plan. In all treatment planning systems, optimization is based on ROI specific cost functions. An optimization function is defined for a ROI, whose dose parameters are set to fulfill certain conditions. For organs at risks, it is common to use certain objectives such as a maximum value for the $D_{2\%}$ or the mean dose. Examples for different types of optimization functions can be seen in Table 3.1, where the functions useable in the program RayStation are listed. As long as they are not set as constraints that have to be fulfilled no matter the circumstances, optimization objectives come with a weighting parameter that defines their relative importance compared to the other functions [68]. The optimization functions can be specified for individual beams, which results in single-field optimization plans. Alternatively, the plan can be optimized for all beams at once by using multi-field optimization (see also chapter 2.5). When using treatment planning software supporting it, the optimization functions can also be set as robust within a certain range of scenarios as defined by the robustness settings (Fig. 3.1).

Optimization Objective	ROI	Description
Minimum Dose	Target	Defines the minimum dose for every voxel in the ROI.
Maximum Dose	Target + OAR	Defines the maximum dose that any voxel in the ROI is allowed to be exposed to.
Uniform Dose	Target	Puts an uniformity objective on the ROI, aiming for the same dose in every voxel.
Minimum DVH	Target	Defines the minimum volume (in %) which has to be covered by the specified dose.
Maximum DVH	Target + OAR	Defines the maximum volume (in %) that can be covered by the specified dose.
Minimum EUD	Target	Minimum equivalent uniform dose. Similar as minimum dose, with an additional parameter A which defines how strongly the optimization algorithm considers 'cold spots', that is areas with a low local dose.
Maximum EUD	Target + OAR	Similar to maximum dose, with the parameter A determining the influence of 'hot spots'.
Dose Fall-off	External	Settings are starting dose, end dose, and distance in which the dose fall-off is supposed to occur.

Table 3.1.: Optimization functions in RayStation 4.8.102.

3.2.1. Robust optimization

Robust Optimization is an optimization method specifically developed for proton therapy. Rather than using the classical idea of a PTV to account for errors, the robust optimization algorithm instead calculates the worst case scenario under a given range for isocenter shifts and density perturbations. The isocenter shift should account for the same positioning and movement uncertainties as in the PTV concept, while the density perturbation corresponds to the range uncertainty caused by systemic uncertainties in the ED-HU calibration curve. By design, robust optimization is therefore supposed to yield similar target coverage under the influence of errors with less dose given to healthy tissue. The basis for the robust optimization used is the minimax optimization, which has the aim of reducing the penalty in the worst case scenario. The scenarios that are considered are a discrete set of scenarios that represent the error margins within which the optimization functions should be robust. Their number depends on the errors that are specified prior to optimization, with each scenario determining a specific setup and density error. As it is the worst case scenario being considered, there is no need to weight the scenarios after their probabilities. However, that means that including too improbable scenarios will invariably reduce the lower plan quality, as the algorithm will try to compensate for every scenario. As such, the scenarios to be included in the optimization have to be chosen carefully. The setup and density errors should be comparable to the errors that can be expected from the specific uncertainties, and not be defined too high [33].

Choosing the maximal errors that are to be considered defines an interval in which robustness should be achieved. Such an interval corresponds roughly to the margins that are used to form the PTV. Therefore, no additional margin around the CTV is needed. Using robust optimization instead of conventional margins has the main advantage of adding less superfluous dose caused by enlarging the target volume by a margin. By directly considering possible scenarios, the actual effects of the errors are better represented. For example, the presence of density errors will mainly lead to shifts of the dose distribution in the direction of the beam. Conventional margins with a uniform margin have to take that into account, but will therefore overshoot in lateral direction of the beam.

To use robust optimization, at least one robust optimization objective has to be specified. The worst case scenario is one in which the robust function has the highest value. In the common case of having more than one robust function, the weighted sum of those functions is considered instead. As the aim is the minimization of that function or sum of functions, the optimization problem can

be expressed in the following form.

$$minmax \sum_{i=1}^{n} w_i f_i(d(x;s)) \tag{3.1}$$

The n functions f_i are the required robust functions with their respective weights w_i, depending on the dose distribution $d(x,s)$. The dose distribution itself is a function of the scenario s within S and the variables x within X, which can be any feasible set of variables (for instance spot weights) [33].

3.3. RayStation

RayStation is a TPS developed by RaySearch Laboratories (Stockholm, Sweden) [69]. It supports photons (IMRT, 3D-CRT and VMAT), electrons, protons and since recently also carbon ions, for which MedAustron is the first customer. The software has certain advantages for proton therapy, as it has implementated certain functions that are not available in most commercial software. Examples are the implementation of multi-criteria optimization, which was originally developed for VMAT/IRMT, and robust optimization. Apart from RayStation Planning, the RayStation package also includes the modules RayPhysics, which is a separate workspace used for beam modeling, and RayBiology, which provides tools for biological optimization and evaluation.

RayStation is divided in a number of modules which serve different functions. The basic handling of the patient data takes place in the patient management module, where the patient information can be edited and DICOM data can be imported or exported. Structure delineation can be done in the structure definition module, where creation and editing of ROIs is possible. Various functions regarding the expansion or reduction of ROIs by margins as well as the possibility to intersect or combine ROIs simplify the creation of ROIs. Noteworthy is also the recent implementation of beam-specific margins. Another module contains the tools for image registration, which can be performed either rigidly or deformable. The deformable registration is based either on the delineated ROIs alone or the ROIs in combination with the density information.

The treatment plans are created in the module plan design, where the treatment modality and various beam parameters are selected. The optimization takes

place in the module plan optimization, where robust optimization with the minimax method can be performed. The remaining modules include plan evaluation, fallback planning, automated planning, adaptive planning and quality assistance preparation. A few of RayStation's specifics, especially in regards to robust optimization are presented in more detail below.

3.3.1. Implementation of robust optimization in RayStation

The robust optimization objectives form a robust optimization problem, which has to be solved. To have continuous gradients of the robust optimization problem, the maximum operator in the equation is approximated by the smooth power mean operator. The actual optimization problem that is solved in RayStation therefore takes the following form, where $d(x, s)$ is the dose distribution and S is the set of scenarios, with the power p set to 8 [70].

$$min(\frac{1}{|S|}\sum_{i\in S}(\sum_{i=1}^{n} w_i f_i(d(x;s)))^p)^{\frac{1}{p}} \tag{3.2}$$

The set of scenarios build the frame within which the chosen objective functions should be robust. Their number and nature is determined by the maximum errors for isocenter shift and density perturbation which occur during patient setup and dose calculation and the robustness settings. Additionally, it is possible to choose whether the different beams should be considered independently. Generally speaking, the amount of overall scenarios depends on the number of setup error scenarios and the number of range error scenarios. If n_s setup error scenarios and n_d density error scenarios are considered, the overall amount of scenarios will be $n_s n_d$.

The setup error scenarios depend on the positioning uncertainties in the robustness settings. With the setup uncertainties u_1, u_2, ..., u_6 (cm) for the 6 directions, the number of scenarios are determined using the following set of rules.

- The nominal scenario, where all positioning errors are 0, is always included
- The scenarios shifted by the maximum positioning errors u_i in their respective direction i are also always included. Between the nominal scenarios and the shift in u_i centimeters, m intermediate scenarios are added, where , with [ ] denoting gaussian brackets and ϵ being an infinitesimal number > 0.

Therefore, intermediate scenarios are only added in the directions for which u_i is strictly larger than 0.75 cm.

- In the 8 directions $(\pm 1, \pm 1, \pm 1)$, the maximum error scenario is computed by forming the ellipsoid which has u_i as its radii. If the resulting setup errors are strictly larger than 0,5 cm, those scenarios are included. Additionally, an intermediate scenarios are added for each 0,75 cm this distance exceeds 0.5 cm.

- In the 12 directions $(0, \pm 1, \pm\phi)$, $(\pm 1, \pm\phi, 0)$ and $(\pm\phi, 0, \pm 1)$, where ϕ is the golden number, a similar process is performed. If the setup errors in those direction, computed as lying on the same ellipsoid, are strictly larger than 1 cm, those scenarios are included. For each 0.75 cm they exceed 1 cm, another intermediate scenario is included.

The number of density scenarios depends on the chosen density perturbation r and is determined with the following formula.

$$n_d = 1 + 2[1 + \frac{1}{5 + \epsilon}] \tag{3.3}$$

Those density error scenarios are spaced evenly in the interval between $-r$ and r. Together, the amount of total scenarios is $n_s n_d$ for dependent beams and $n_s^b n_d$ for independent beams, if b is the number of existing beams. Regarding the beams independently leads to a large amount of scenarios and high computation time due to the exponential nature of $n_s^b n_d$ [70].

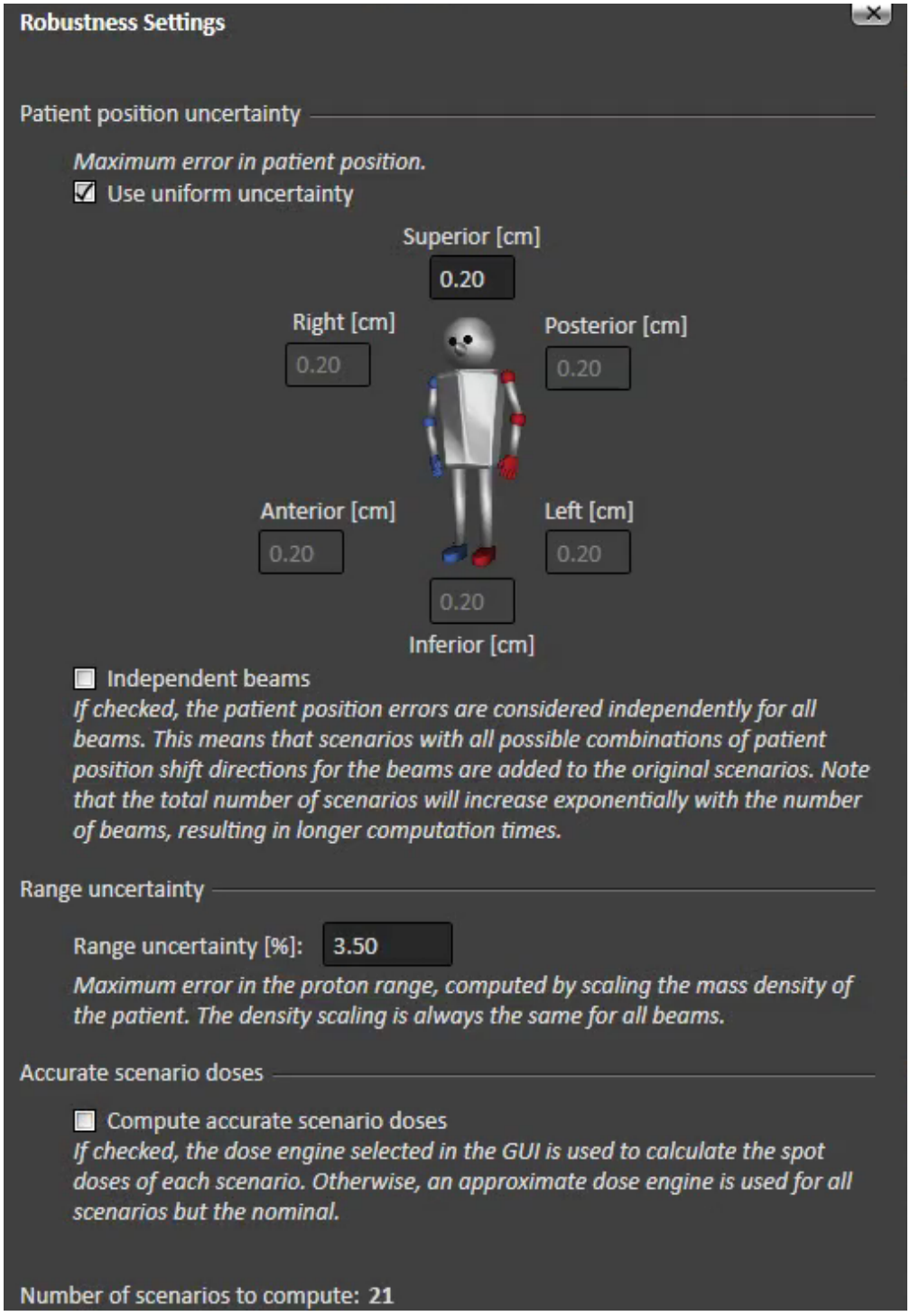

Figure 3.1.: Robustness setting in RayStation.

4. Materials and Methods

4.1. Study design

The overall purpose of this thesis was to examine alternative margin concepts in proton therapy for pediatric ependymoma patients and compare their performance under the influence of positioning and density uncertainties. For this purpose the clinically used CTV expansion margin of 5mm was reduced to 2mm and replaced by beam-specific margins. Beam-specific margins also use a PTV to ensure reliable CTV coverage, but use different margins dependent on the direction of the beam. Enhanced distal margins were used to account for the range errors.

Another alternative is robust optimization, an optimization algorithm originally developed for proton therapy. Rather than using the classical idea of a PTV, the robust optimization algorithm instead calculates the worst case scenario under a given range for isocenter shifts and density perturbations. It then uses the minimax function to optimize by trying to fulfill the robust optimization objectives even in the perturbed scenarios. By design, robust optimization is therefore supposed to yield similar target coverage while sparing healthy tissue. As robust optimization can be applied to each optimization goal individually, it is possible to only use robust optimization for the target volume, namely the CTV; or to also apply it to any number of OAR objectives. Both options were explored to see whether additional robust optimization objectives give a significant advantage.

The study itself was conducted at the Medical University of Vienna working as research unit at the non-clinical research part, PEG, of MedAustron in Wiener Neustadt, Austria, using the treatment planning software RayStation (Raysearch, Sweden). As the original treatment plans were created with a different treatment planning system, they first had to be recreated. All treatment plans were created using single field optimization, with energy layer spacing of 0.5 cm and spot spacing of 0.3 cm. The optimization was performed with a maximum of 100 iterations. After 20 iterations, spot filtering by introducing a minimum spot weight of 0.001

MU/fx took place.

To perform the robust evaluation, it was necessary to calculate the perturbed doses for a certain amount of error scenarios, in this case 20 scenarios for each nominal plan. As the summed plans resulting from the addition of the individual series, of which there were four for each patient, had to be considered as well, nearly 4000 perturbed dose scenarios were calculated with this study.

These numbers necessitate the at least partial automation of the robust evaluation process. This is achieved by making use of RayStation's ability to run Python scripts. A robust evaluation tool in form of such a script was designed during the course of this thesis. As it can be used or adapted for any treatment plan created with RayStation, it could serve as an aid for future studies requiring automated robust evaluation. The $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$ for target volumes as well as the $D_{2\%}$ and average dose for OARs were examined. By comparing those values for the different plans under the influence of positioning and density errors, the aim was to make a statement about their robustness.

4.2. Patient collective

Clinical treatment plans for 8 pediatric ependymoma cases served as the basis for the evaluation of the different margin concepts. These patients have been treated at the Paul-Scherrer Institute (PSI) in Villigen, Switzerland, using pencil beam scanning with protons. Their data, including the clinical treatment plans created using PSIplan, has been provided by the PSI in the context of a research cooperation project.

The patients were treated in prone position, with their treatment based on CT images with a slice thickness of 0.2 cm. Each patient was clinically treated by 4 series differing in dose prescription, target volume and beam direction. Therefore, each of those series can be seen as individual plan for the purpose of robust evaluation. In total, 32 treatment plans were compared to their respective comparison plans using different margin concepts. Furthermore, the summed plans were evaluated with respect to clinical OAR constraints (table 4.1).

OAR	mean dose	$D_{2\%}$
Brainstem	54 Gy(RBE)	59.4 Gy(RBE)
Chiasm	50 Gy(RBE)	54 Gy(RBE)
Spinal Cord (below C1)	-	50.4 Gy(RBE)
Optical nerve	-	45 Gy(RBE)
Lacrimal Gland	20 Gy(RBE)	30 Gy(RBE)
Ventral eye	-	36 Gy(RBE)
Lens	7 Gy(RBE)	10 Gy(RBE)
Cochlea	36 Gy(RBE)	45 Gy(RBE)

Table 4.1.: Clinical constraints for OARs relevant to brain tumors.

Clinical Treatment strategy

The overall original treatment strategy foresaw the treatment of the patients with 4 irradiation series with slightly different target volumes, generally using a 5mm margin between CTV and PTV. The summed prescription dose was 59.4 Gy (RBE), delivered in fractions of 1.8 Gy (RBE) as median dose to the respective PTV (illustrated in 4.1). This dose was distributed over the series as follows.

- Series 1: 30.6 Gy (RBE), 17 fractions

  The first and largest series was applied to the PTV, which is the CTV expanded by a 5mm margin. The PTV was further expanded in an non-uniform manner to ensure symmetrical irradiation of bone tissue. This was done because radiation is known to stunt growth, and the asymmetrical growth of the pediatric patients has to be avoided.

- Series 2: 19.8 Gy (RBE), 11 fractions

  The second series was applied to the PTV, without regarding symmetrical irradiation of the bones.

- Series 3: 3.6 Gy (RBE), 2 fractions

  The main purpose of the third series was to spare the spinal cord, as the target volume is generally equal to the PTV in Series 2, but cut off below the first vertebrae of the spinal column.

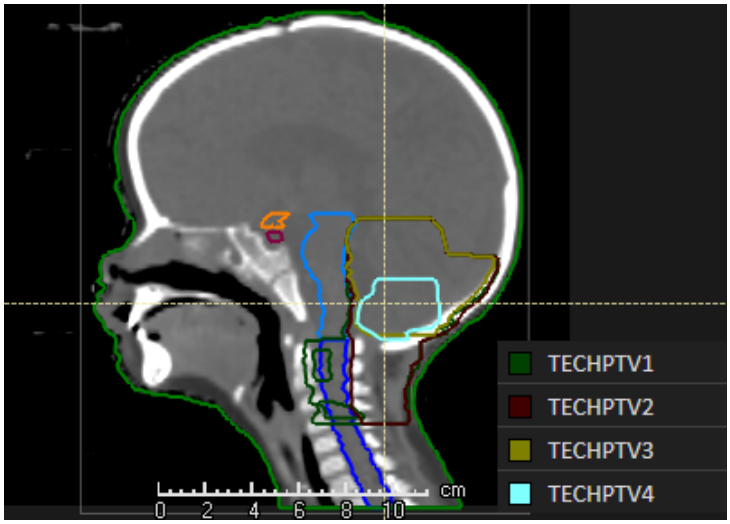

Figure 4.1.: Illustration of the actual target volumes used in the four different treatment series.

- Series 4: 5.4 Gy (RBE), 3 fractions

  The fourth series was an additional boost which serves the main purpose of delivering additional dose to the tumor bed. As such, the GTV served as the CTV for Series 4 and the PTV for Series 4 was the GTV expanded by 5mm.

As the location of the tumor in the patients was intracranial, the relevant organs that had to be spared are the brainstem, spinal cord, chiasm, optic nerves, hippocampus and other organs located in the cranium. The PTV of the patients in this study generally overlapped with the brainstem and spinal cord, as shown in figure 4.2, making proper sparing of those organs particularly difficult. To spare them, the original plans often featured further modulation of the PTV, resulting in so-called TechPTVs. Those modulations were also used in the recreated 5mm margin plans and generally adapted for the plans using 2mm or beam-specific margins. However, as the robust optimization is meant to be applied directly to the CTV, the original form of the CTV was retained for those plans with the following exceptions.

- In Series 3, any target volume regardless of the margin concept was cut below the same plane as the original plan, to maintain the spinal cord sparing.

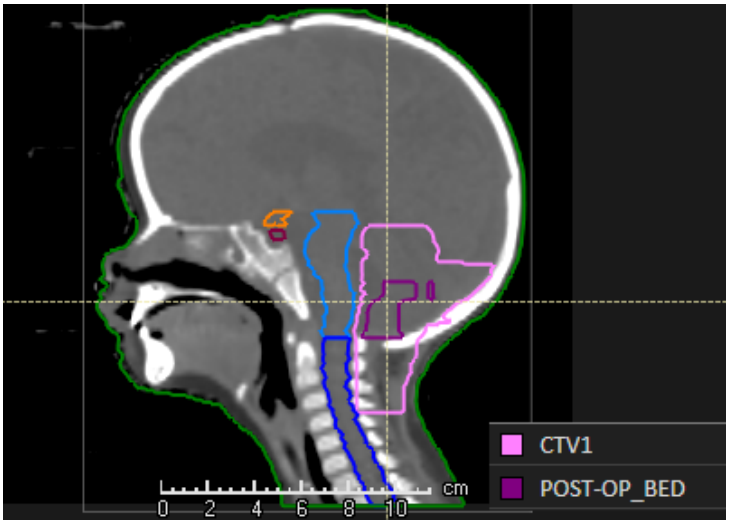

Figure 4.2.: Delineated target volumes for the ependymoma treatment of a representative patient.

- In Series 4, the modulated target volume (TechPTV) was used as basis for the creation of the plans.

As a general rule, the overall treatment strategy was to be preserved even when using alternative margin concepts. The PTVs in Series 1 for the 2mm and beam-specific margins were altered to ensure symmetrical irradiation of the bone, as it was done for the 5mm margins.

4.3. Treatment planning approaches

Optimization Strategy

The optimization was carried out by using a number of optimization objectives. The design of those objectives was fairly consistent between the patients, with no major differences in the general optimization approach. For all RSL plans, the PTV was set to have a minimum dose, maximum dose and uniform dose equal to the description dose. The minimum dose and maximum dose objectives were given a higher relative weight than the uniform dose objective and therefore had a higher impact on the overall target coverage. The standard weighting values

used in this study were 100 for the former and 60 for the latter. As the uniform dose objective was used to avoid hot and cold spots within the target volume, it would sometimes complicate the sparing of the brainstem. Thus, its weighting was lowered further in some cases. If a TechPTV for brainstem sparing was used, the influence of the TechPTV had to be considered as well.

Another objective that was used for every plan is a dose fall-off from the prescription dose to a low dose level (0-10 Gy (RBE)) for the 'External' ROI, with a low relative weight. Even with just a weight of 5 or 10, the dose fall-off is required by the TPS to minimize the dose outside of the target. The exact parameters vary, and were chosen so that the dose fall-off did not become the dominant objective for the optimization.

The objectives for the organs at risk were more varied, depending on the individual anatomy of the patient. For most patients, maximum dose objectives were used to limit their dose exposure, and supplemented by maximum DVH objectives if necessary. Their relative weight depended mostly on their proximity to the tumor and therefore the effort needed to spare them. The exact values used range from 5 to 45. Lower values were sufficient for organs at a remote distance to the tumor, as they were at little or no risk of exceeding their tolerance dose limit. Examples include the optical nerves, pituary gland, hypothalamus, lacrimal glands, eyes, lenses, and temporomandibular joints. In cases where the organ was too far away from the beam paths to receive any dose, no objective for that organ was used at all. Organs that were generally more difficult to spare include the brainstem, spinal cord and to a lesser extent chiasm, hippocampus as well as middle and inner ears. Especially for the brainstem and spinal cord the use of multiple, more heavily weighted objectives were necessary in several cases. In very few instances, a maximum EUD objective was used to guarantee that the brainstem did not suffer from local hot spots. For the other OARs, the maximum dose objective in combination with at most a single maximum DVH objective was found to be sufficient.

Recreation of the clinical treatment plans (5mm margin)

The primary goal for the recreation of the clinical treatment plans with 5mm CTV to PTV margin was to achieve a comparable target coverage and OAR sparing as the original plans. In cases where the plans created with RayStation (RSL plans) yielded slightly better coverage, such as a $D_{98\%}$ higher by less than 0.3 Gy (RBE), the discrepancy to the original plan was accepted.

2mm margin plans

The optimization parameters used in the associated RSL plans served as basis for the 2mm margin plans. Further optimization was only undertaken to take advantage of the reduced margins. It is assumed that the RSL plan was already optimized well, and any potential gains in OAR sparing resulted from the use of another margin concept and not from the additional optimization effort of the treatment plan itself. This holds true for all plans using alternative margin concepts that were investigated.

Beam-specific margin plans

For the beam-specific (BS) margin plans, a distal margin of 5mm, proximal margin of 2mm and lateral margins of 2mm were chosen. The enhanced distal margin is to account for the influences of density perturbations, meaning uncertainties in the range of the proton beam. It can be argued that the proximal margin should be enhanced as well, as the dose distribution in beam direction is affected the most. However, as the distance between the beam entry point and the proximal edge of the CTVs was relatively small for all patients, the disturbance of the dose distribution at that edge was deemed not large enough to warrant a larger margin. The main idea behind using beam-specific margins is to eliminate some of the superfluous target volume that arises from using uniform margins. In order to carry out the optimization with beam-specific margins, it was necessary to create a beam-specific PTV for each beam, of which there were usually 3 (Fig. 4.3. Each objective which would pertain to the PTV in the RSL plan had to be split into 3 individual objectives, each set to a single beam and the respective beam-specific PTV. Accordingly, the dose level of those objectives was one-third of the prescription dose for an individual objective. As such, a Series 1 RSL plan with objectives for the maximum dose, minimum dose and uniform dose at 30.6 Gy (RBE) would lead to a beam-specific plan with 3 sets of those objectives at 10.2 Gy (RBE). The relative weight settings were mostly unchanged from the RSL plans. As the use of BS margins necessitates the individual optimization of the beams, only SFO plans could be created with this approach.

Robust optimization CTV

Two robust optimization approaches were investigated. In both of them, the minimum and uniform dose objective to the CTV were set as robust, as they are meant to ensure sufficient target coverage. In this approach the robust optimization was applied only to those two objectives. The robust optimization settings were 2mm uniform isocenter shift and 3.5% density perturbation, mirroring the values used for robust evaluation. The prescription dose was always applied to the unmodulated CTV, with the only exception being the cut-off of the lower area to spare the spinal cord in Series 3 and 4. For Series 4, the clinical target volume was generally equal to the GTV.

Robust optimization CTV + OAR

This margin concept was chosen to further investigate the influence of robust optimization when applied specifically to the OARs that should be spared. For purpose of better comparison, the optimization parameters differed between the two approaches only in the fact that the maximum dose objectives for brainstem and chiasm were set as robust. Dose level, relative weighting and the objectives for all other OARs and the CTV stayed the same. As the brainstem was directly affected by the tumor, it received high doses and sparing of the healthy brainstem tissue was difficult. Robustness of the plan was therefore particularly important and these settings were meant to improve it. Robust optimization objectives applied to the chiasm were meant to investigate their effect on OARs further away from the primary tumor. For the purpose of distinguishing between the two robust optimization approaches, the approach including the OARs was denoted as 'RobustB' in the results.

4.4. Plan evaluation

The evaluation was based on certain points in the DVH of the plans, namely the $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$ of the CTV, as well as the $D_{2\%}$ and average dose of OARs. As the robust optimization uses a prescription to the CTV, only the CTV rather than any PTV could be chosen as meaningful measure of comparison. To compare the different margin concepts, both the nominal plans and their respective perturbed plans had to be evaluated. The nominal plans were compared by their

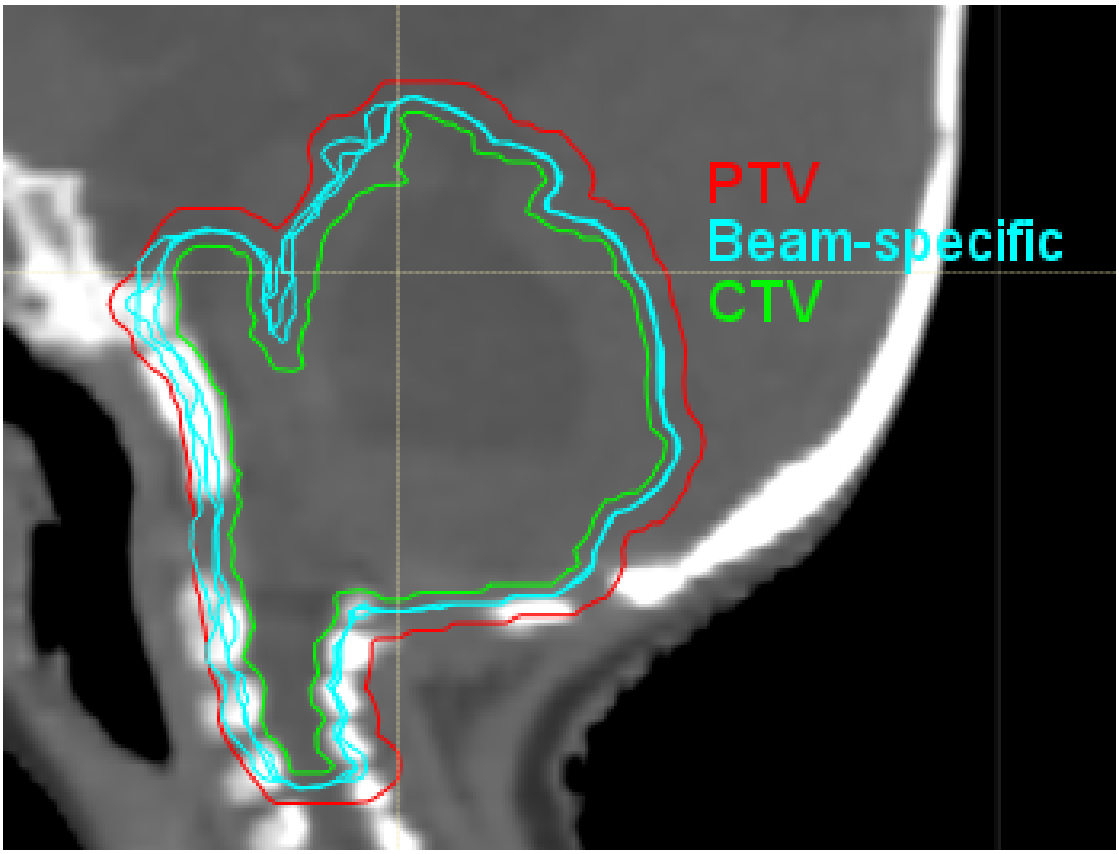

Figure 4.3.: The beam-specific margins were implemented by creating PTVs corresponding to the treatment beams.

fulfillment of the prescription dose ($D_{50\%}$ of CTV), their target coverage ($D_{98\%}$, $V_{95\%}$) and their sparing ($D_{2\%}$, mean dose). Thus, high plan quality is marked by OARs having low values for $D_{2\%}$ and the mean dose. Meanwhile, the CTV/PTV should have high values for $D_{98\%}$ and $V_{95\%}$ as well as a close adherence of $D_{50\%}$ to the description dose. Their summed plans were used to determine whether any clinical constraints were exceeded by the full treatment consisting of 4 Series.

4.5. Robust evaluation

The evaluation of the plans' robustness was carried out by calculating the perturbed plans. The perturbation settings allow for the choice of the isocenter shift and the density perturbation, which are used to calculate the perturbed dose distribution for a specific scenario. The scenarios chosen for investigation were ±2mm isocenter shifts in the six coordinate directions combined with density shifts of 0% and ±3,5%. As the scenarios with only density, but no isocenter shift were included, this resulted in 20 perturbed scenarios in addition to each nominal plan. To perform robust evaluation for the summed plans, it would have been necessary to examine the robustness depending on fractionation voxel by voxel. Therefore, the robust evaluation was only performed for the individual series, and not for the summed up plans. However, the summed plans were used to see if any clinical constraints for OARs (Table 4.1) were exceeded.

4.5.1. Evaluation script

In order to perform the robust evaluation of the different treatment plans, a Python script was written. Using this script, the plans were evaluated by calculating the perturbed doses arising from given isocenter shifts and density perturbations. Target coverage and OAR sparing were compared by taking the $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$ for target volumes as well as the $D_{2\%}$ and the mean dose for organs at risk. For each organ and each plan the minimum, maximum and mean of those values over the error scenarios were calculated. While the multiple series for each patient were technically treated as individual plans for the purpose of evaluation, the summed plans were also created. By adding up both the nominal plans, it was possible to see whether any clinical constraints have been exceeded. All of the aforementioned data was saved by writing it into a csv-file.

4.5.2. Script usage

For the script to run successfully and correctly, a few prerequisites have to be fulfilled. First of all, the evaluated patient has to be currently opened in RayStation when running the script. While performing the necessary calculations for more than one patient was thereoretically possible, it would be more prone to unforeseen circumstances and lead to a loss in flexibility. As the script is meant to serve as a tool for robust evaluation beyond this study alone, a certain degree of flexibility and simplicity is advantageous.

To use the script, it is necessary to follow several rules regarding the nomenclature of the plans. The individual plans subject to evaluation are specified by name in the code. As such, the name of the treatment plan in RayStation has to match the name in the code. Likewise, the ROIs to be evaluated have to specified and a selection mechanism was implemented.

In RayStation, it is possible to designate the type and organ type of each ROI. While the type (PTV, CTV, Organ, etc.) is important for the optimization process, the organ type serves no planning or optimization process in this study. Therefore, the organ type is used as a marker to indicate whether a certain ROI is to be evaluated. If it is set to "Target", the $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$ of the ROI will be determined. If it is set to "Organ at Risk", the $D_{2\%}$ and mean dose will be calculated. In case it is set to anything else, the ROI will be skipped.

At the end of the script, it will by default delete all evaluation doses (perturbed and summed doses) as their sheer number puts a considerable strain on the planning software. A function to preserve preexisting evaluation doses was implemented in case it was considered to be necessary.

4.6. Robust evaluation script

As the script is tailored towards use with the specific cases in this study, its structure will be explained in detail to make it more accessible for general use.

```
from connect import *

#IMPORTANT: Change organ type of ROIs you want no data of to Unknown!
(Alternatively,
manually edit used_rois)
#Alternative: Write ROIs to be used in used_rois below.

patient = get_current("Patient")
case = patient.Cases[0]

#Isocenter shift:
shift = 0.2
#Density Perturbation:
sigma = 0.035

xshift = [shift, -shift, 0.0, 0.0, 0.0, 0.0, 0.0]
dsigma = [sigma, -sigma, 0.0]
group = ['2mm', 'BS', 'RSL', 'Robust', 'RobustB']

rois = case.PatientModel.RegionsOfInterest
relevant_types = ["Target", "OrganAtRisk"]

#ROIs to be analyzed
#used_rois = ["BRAINSTEM", "CHIASM", "CTV=GTV2=10MM_MOD", "EYE_L",
    "EYE_R", "HIPPOCAMPUS_L", "HIPPOCAMPUS_R", "HYPOTHALAMUS",
    "INNER_EAR_L", "INNER_EAR_R", "LENS_L", "LENS_R", "MIDDLE_EAR_L",
    "MIDDLE_EAR_R", "OPTIC_NERVE_L", "OPTIC_NERVE_R", "PAROTID_L",
    "PAROTID_R", "PITUARY_GLAND", "SPINAL_CORD", "EXTERNAL"]
```

After accessing the currently opened patient, the first part of the code mainly defines a number of variables that are necessary for its operation. The isocenter shift and density perturbation for the perturbed dose scenarios are defined at the beginning, partly because they are meant to be easily accessible. Due to the specifications of RayStation, the isocenter shift is given in centimeters, while the density perturbation is written as a fraction of one. As the isocenter shifts are to be examined in all directions and for positive and negative density perturbations, the corresponding lists are used to cycle through the different permutations. Using these lists, all twenty error scenarios to each nominal plan will be calculated. In a similar manner, the list called 'group' is used to create the 5 summed plans for each patient.

The term 'rois', as well as the term 'case' above, are simply used as an abbreviation to make the remainder of the code easier to read.
The line 'case.PatientModel.RegionsOfInterest' is not a specific command, but just part of the overall structure of the patient that refers to his regions of interest. It is possible to see the way a patient and its plans are structured and the correct functions to address them by launching the state tree, which would be done with a separate script.

In case the organ type is relevant for any reason and therefore can't be used as a marker anymore, another option to select for the ROIs to be evaluated can be used. Writing them into a list that defines the used ROIs is a time-consuming and slightly more error-prone method, but possible as an alternative. It is recommended to only resort to it if the correct organ type is actually important.

```
def getid(obj):
  s = obj.__repr__()
  return s[s.find("id=")+3:-1]

doseID = []
weight = []
Pr = []

for i in range(105):
  doseID.append([])
for i in range(5):
  weight.append([])
  Pr.append([])
```

The above part contains a function and several variables used to create the summed plans. The getid-function returns the ID-number of an evaluation or planning dose in RayStation, which is necessary to perform the SumDose command. It should be noted that this method of retrieving the ID is more of a trick rather than formally implemented, and it is likely that a proper command will appear in future versions of RayStation. The dose-IDs are stored in the equally named lists. As the aim is to calculate 20 error scenarios for every nominal plan, and there are 5 types of plans whose margin concepts are investigated, there are 105 of these lists in total. Any single list will store the ID of the plans with a given margin concept and error scenario. As an example, doseID[0] will contain the IDs of the nominal 2mm plans, which result in the 2mm plan for the entire patient when summed up. As the first element of that list, doseID[0][0] will be the ID of the Series 1 2mm plan, while

doseID[0][3] will be the ID of the Series 4 2mm plan (if 4 or more series exist). The number of IDs stored in a list therefore reflects the number of series for a patient.

In a similar manner, the lists called 'weight' and 'Pr' are used to store the number of fractions and the prescribed doses for each plan. Those values are also necessary to compute the summed dose, but as they stay the same for the error scenarios, having only 5 of those lists is enough. Technically it would be sufficient to have just one list for this study, as the different margin concepts all use the same fractionation and prescriptions. However, as this might not be the case for future cases, the summing up was implemented in this more basic manner.

```
potential_plans = ["Series 1 2mm", "Series 1 BS", "Series 1 RSL",
    "Series 1 Robust", "Series 1 RobustB", "Series 2 2mm", "Series 2 BS",
    "Series 2 RSL", "Series 2 Robust", "Series 2 RobustB", "Series 3
    2mm", "Series 3 BS", "Series 3 RSL", "Series 3 Robust", "Series 3
    RobustB", "Series 4 2mm", "Series 4 BS", "Series 4 RSL", "Series 4
    Robust", "Series 4 RobustB", "Series 5 2mm", "Series 5 BS", "Series 5
    RSL", "Series 5 Robust", "Series 5 RobustB"]

used_plans = []

for i in range (case.TreatmentPlans.Count):
  if case.TreatmentPlans[i].Name in potential_plans:
    used_plans.append(case.TreatmentPlans[i].Name)

used_plans.sort()

fout = open('{}.csv'.format(patient.PatientID), 'w')
fout.write("Patient: {} \n".format(patient.PatientID))
```

The standard treatment approach for the ependymoma patients in this study consisted of 4 series. To ensure that the only the intended plans are used, a list of potential plans exists, and only plans with a name equal to a member of that list will be used. As the plans are checked in the order in which they were created, the used plans are afterwards sorted alphabetically to put them in the correct order for future operations.

The results of the evaluation are saved in a csv-file (comma separated values file), which has the distinct advantage of being openable by Excel or similar programs as a decently formatted table. The name of the created file is the PatientID assigned

to the currently opened patient in RayStation.

```
for i in range (len(used_plans)):
  plan = case.TreatmentPlans[used_plans[i]]
  beam_set = plan.BeamSets[0]
  structure_set = plan.GetStructureSet()

  #manually enter the rois to be used in used_rois if preferred
  roi_names = [roi.OfRoi.Name for roi in structure_set.RoiGeometries if
      roi.OfRoi.OrganData.OrganType in relevant_types]
  #roi_names = [roi.OfRoi.Name for roi in structure_set.RoiGeometries if
      roi.OfRoi.Name in used_rois]
  fr = plan.TreatmentCourse.TreatmentFractions.Count
  P = beam_set.Prescription.DosePrescriptions[0].DoseValue
  Pr[i%5].append(P)

  fout.write("\n")
  fout.write("Plan: {}, ".format(plan.Name))

  examination_name = plan.GetStructureSet().OnExamination.Name
  fraction_number = 0

  doseID[0+(21*(i%5))].append(getid(beam_set.FractionDose))
  weight[(i%5)].append(fr)
```

The part of the code that iterates over the used plans is responsible for calculating the perturbed doses of the plan, writing the results to the aforementioned csv-file and saving the necessary data needed to create the summed plans. Firstly, a few variables are defined to basically serve as abbreviations to make the remainder of the code simpler. The definition of roi_names should correspond to the chosen method of distinguishing between relevant and irrelevant ROIs. In regard to the future creation of the summed plans, the doseID, fraction count and prescription dose are appended to the appropriate lists.

As the used plans have been sorted alphabetically, the order in which the plans are processed is the following: “Series 1 2mm”, “Series 1 BS”, “Series 1 RSL”, “Series 1 Robust”, “Series 1 RobustB”, “Series 2 2mm”, etc.

Using that preestablished order, the modulo operator (%) is used to save the doseID, fraction count and prescription dose in the correct list. As this part of the

code only refers to the nominal plan, only the corresponding doseID lists are used. The reason for the separate treatment of nominal and perturbed plans mainly lies in RayStation handling them slightly differently. Most noticeably, the commands to access the dose vary.

```
for j, roiName in enumerate(roi_names):
  if rois[roiName].OrganData.OrganType == 'Target':
    doseAtRelVol.append(plan.TreatmentCourse.TotalDose.
    GetDoseAtRelativeVolumes(RoiName = roiName, RelativeVolumes =
        [0.02, 0.50, 0.98]))
    RelVolAtDose.append(plan.TreatmentCourse.TotalDose.
    GetRelativeVolumeAtDoseValues(RoiName = roiName, DoseValues =
        [P*0.95]))
  elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
    doseAtRelVol.append(plan.TreatmentCourse.TotalDose.
    GetDoseAtRelativeVolumes(RoiName = roiName, RelativeVolumes =
        [0.02]))
    RelVolAtDose.append(0)

for j, roiName in enumerate(roi_names):
  if rois[roiName].OrganData.OrganType == 'Target':
    fout.write("{0},,,, ".format(roiName))
  elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
    fout.write("{0},, ".format(roiName))
fout.write("\n")
for j, roiName in enumerate(roi_names):
  if rois[roiName].OrganData.OrganType == 'Target':
    fout.write(", D2%, D50%, D98%, V95%D")
    Calc.append([])
    Calc.append([])
    Calc.append([])
    Calc.append([])
  elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
    fout.write(", D2%, Avg")
    Calc.append([])
    Calc.append([])
fout.write("\n x: 0; y: 0; z: 0; d: 0%")
for j, roiName in enumerate(roi_names):
  if rois[roiName].OrganData.OrganType == 'Target':
    fout.write(", {}, {}, {}, {}".format(doseAtRelVol[j][0],
        doseAtRelVol[j][1], doseAtRelVol[j][2], RelVolAtDose[j][0]*100))
  elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
```

```
      fout.write(", {}, {}".format(doseAtRelVol[j][0],
          plan.TreatmentCourse.TotalDose.GetDoseStatistic
(RoiName = roiName, DoseType = "Average")))

  fout.write("\n")
```

Before the perturbed doses are calculated, it is first necessary to evaluate the unperturbed dose. For the purpose of evaluation, the relevant data points are $D_{2\%}$, $D_{50\%}$, $D_{98\%}$, $V_{95\%}$ and the mean dose. The lists doseAtRelVol and RelVolAtDose are used to store the values for doses at certain relative volumes and the relative volume at a certain dose. The list Calc is an auxiliary list which is later used to determine the maximum, minimum and mean values of $D_{2\%}$, $D_{50\%}$, $D_{98\%}$, $V_{95\%}$ and the mean dose for the error scenarios. Using the enumerate function, the relevant doses and volumes are then determined for every used ROI. The lines following thereafter are mostly used to write the results to the csv-file. As the unperturbed doses are not included in the average values for $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$, Calc is up to now only a list consisting of empty lists. Each of those empty lists corresponds to a column in the csv-file, in which the values of a certain data point (such as the $D_{2\%}$ for the brainstem) will be stored and can be used to calculate the average.

```
  for k in range (20):
    x = xshift[((k+19)//3)%7]
    y = xshift[((k+34)//3)%7]
    z = xshift[((k+49)//3)%7]
    d = dsigma[k%3]

    isocenter_shift = {'x':x, 'y':y, 'z':z}
    beam_set.ComputePerturbedDose(ExaminationNames=[examination_name],
        FractionNumbers=[fraction_number],
        IsocenterShift=isocenter_shift, DensityPerturbation=d)

    dose=case.TreatmentDelivery.FractionEvaluations[0].
    DoseOnExaminations[0].DoseEvaluations[case.TreatmentDelivery.
    FractionEvaluations[0].DoseOnExaminations[0].DoseEvaluations.Count-1]
```

The previously defined lists xshift and dsigma are used to calculate the perturbed doses of the current plan. By using the modulo operator (%) and division without remainder (//), the variables x, y, z and d, which define the actual isocenter shift

and density perturbation used for a given perturbed dose, cycle through the values in those lists. With the chosen setup, first the two scenarios without an isocenter shift, but with density perturbations will be calculated. Next are the three scenarios with a positive shift in the x-direction and varying density perturbation, then the three scenarios with a negative shift in the x-direction. Doing the same for the other two axis results in the 20 different perturbation scenarios, of which each is handled in one iteration of this part of the script. Because RayStation does not allow the computation of an unperturbed dose with the same command that computes the perturbed doses, it is necessary to handle the unperturbed dose separately, as described above. In the script, the term "dose" is an abbreviation for a command that accesses the evaluation doses, which in this case are the perturbed doses, that have been calculated. By design, it always refers to the evaluation dose that has been created last, and its definition is updated with every iteration.

```
    doseID[k+1+(21*(i%5))].append(getid(dose))
    doseAtRelVol = []
    RelVolAtDose = []
    v = 0

for j, roiName in enumerate(roi_names):
      if rois[roiName].OrganData.OrganType == 'Target':
        doseAtRelVol.append(dose.GetDoseAtRelativeVolumes(RoiName =
            roiName, RelativeVolumes = [0.02, 0.50, 0.98]))
        RelVolAtDose.append(dose.GetRelativeVolumeAtDoseValues(RoiName =
            roiName, DoseValues = [P*0.95/fr]))
      elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
        doseAtRelVol.append(dose.GetDoseAtRelativeVolumes(RoiName =
            roiName, RelativeVolumes = [0.02]))
        RelVolAtDose.append(0)

    fout.write("x: {}; y: {}; z: {}; d: {}%".format(x, y, z, d*100))

    for j, roiName in enumerate(roi_names):
      if rois[roiName].OrganData.OrganType == 'Target':
        fout.write(", {}, {}, {}, {}".format(doseAtRelVol[j][0]*fr,
            doseAtRelVol[j][1]*fr, doseAtRelVol[j][2]*fr,
            RelVolAtDose[j][0]*100))
        Calc[v].append(doseAtRelVol[j][0]*fr)
        Calc[v+1].append(doseAtRelVol[j][1]*fr)
        Calc[v+2].append(doseAtRelVol[j][2]*fr)
        Calc[v+3].append(RelVolAtDose[j][0]*100)
        v = v+4
```

```
    elif rois[roiName].OrganData.OrganType == 'OrganAtRisk':
      Avg = dose.GetDoseStatistic(RoiName = roiName, DoseType =
          "Average")*fr
      fout.write(", {}, {}".format(doseAtRelVol[j][0]*fr, Avg))
      Calc[v].append(doseAtRelVol[j][0]*fr)
      Calc[v+1].append(Avg)
      v = v+2

  fout.write("\n")
```

Similarly to the nominal scenario, the ID of the perturbed dose is stored in one of the doseID lists for later summation. The lists doseAtRelVol and RelVolAtDose are cleared with each iteration as they only serve as a simple storage for the data points. However, the list Calc is not cleared as it is used to determine the mean, maximum and minimum values of those data points over all error scenarios. It uses the running variable "v" to add the values to the correct lists, depending on whether the ROI in question has been marked as "Target" or "Organ at Risk".

After the calculation of the perturbed dose, it goes through the same process as the unperturbed dose, with its data points being written into the csv-file. As the script works with the doses given in a single fraction, the doses at relative volumes have to be multiplied with the number of fractions to get the correct dose for the entire perturbed plan. Likewise, the dose level of which the relative volume is determined has to be divided through the number of fractions.

For general usage of the robust evaluation tool in either a clinical or non-clinical scenario, it is usually not necessary to create the summed doses. In cases where the perturbed dose is not needed for further evaluation, it is recommended to delete it within the same iteration it was created in.

```
fout.write("Minimum")
for l in range (len(Calc)):
  fout.write(", {}".format(min(Calc[l])))
fout.write("\nMaximum")
for l in range (len(Calc)):
  fout.write(", {}".format(max(Calc[l])))
fout.write("\nMean")
for l in range (len(Calc)):
  fout.write(", {}".format(float(sum(Calc[l]))/len(Calc[l])))
fout.write("\n")
```

For each ROI, either two (if marked as "Organ at Risk") or four (if marked as "Target") lists have been created, in which the values for the average dose, D2%, D50%, D98% or V95%D are stored. Those lists are utilized to find the minimum, maximum and average of those values under the different error scenarios, which are written into the csv-file directly under the corresponding columns.

```
for b in range(5):

  case.SumDoses(DoseName = '{} 0% 0 0 0'.format(group[b]), FractionNumber
     = 0, Doses = doseID[0+(21*b)], Weights = weight[0])
   dose=case.TreatmentDelivery.FractionEvaluations[0].DoseOnExaminations[0]
       .DoseEvaluations[case.TreatmentDelivery.FractionEvaluations[0]
.DoseOnExaminations[0].DoseEvaluations.Count-1]
  doseAtRelVol = []
  RelVolAtDose = []
  Calc = []
  fout.write("\n")
  fout.write("Plan: {} Sum, ".format(group[b]))

  fout.write("Minimum")
  for l in range (len(Calc)):
    fout.write(", {}".format(min(Calc[l])))
  fout.write("\nMaximum")
  for l in range (len(Calc)):
    fout.write(", {}".format(max(Calc[l])))
  fout.write("\nMean")
  for l in range (len(Calc)):
    fout.write(", {}".format(float(sum(Calc[l]))/len(Calc[l])))
  fout.write("\n")
```

After all nominal and perturbed single-series doses have been handled, the design of the original treatment plans necessitates the summation of those plans. The stored IDs and fraction weights of the doses are necessary to create the summed plans with the "case.SumDoses" command. As there are five margin concepts whose robustness is to be evaluated, five summed doses for the nominal cases are created. Even though they are not used for robust evaluation, the perturbed summed doses are calculated as well.

```
while True:
  if case.TreatmentDelivery.FractionEvaluations[0].DoseOnExaminations[0]
.DoseEvaluations.Count > 0:
    case.TreatmentDelivery.FractionEvaluations[0].DoseOnExaminations[0]
.DoseEvaluations[case.TreatmentDelivery.FractionEvaluations[0]
.DoseOnExaminations[0].DoseEvaluations.Count-1].DeleteEvaluationDose()
  else:
    break
```

During the course of its operation, the script creates nearly 4000 evaluation doses. At this number of doses, their existence is enough to make RayStation basically inoperable, making it important to delete them at the the end. The final lines shown above delete all evaluation doses regardless of whether they were created by the script itself or not. In the case of preexisting evaluation doses, for instance a manually created summed plan, the number of doses to be preserved, namely the condition of the if-clause, has to be changed.

Overall, the runtime of the script depends heavily on the details of the evaluated patient. Bigger volumes, more ROIs and having the full amount of series will lead to a significantly higher computation time. While it took only 4 hours to perform the robust evaluation for the patient with only 2 series and therefore less plans, the longest operation time was approximately 40 hours. For general usage, such times would be very inconvenient in a non-clinical setting and unacceptable in a clinical one. However, unlike in this study, it usually won't be necessary to calculate the summed doses or this amount of perturbed doses.

The time needed for computation does not increase linearly with the amount of evaluation doses that need to be calculated, as the storage of data in memory slows down the operation. That effect is amplified by the need to create the summed doses, which also requires the retention of the individual perturbed doses until their summation. A detailed investigation concerning the operation time has not been performed, but a few benchmarks have been taken. Running the full script for the involved patients takes up to 40 hours, while running the script without the creation of the summed plan takes roughly 25 to 30 hours. Without the summed plans and with one less margin concept, the time is reduced under 20 hours. In the simplest case, which would be the robust evaluation of a single plan, the operation takes a few minutes at most. Assuming that the amount of plans to be evaluated stays at a manageable number, the robust evaluation tool should also be suitable for clinical purposes.

It is also possible to further cut down the time needed by reducing the amount of error scenarios to be considered and by evaluating less ROIs. The scenarios with only density perturbation and no isocenter shift as well as the ones with no density perturbations were included in this study to gain more information about the robustness of the different plans. They are not strictly necessary in cases where the robust evaluation is performed to see whether any clinical constraints are broken in the worst scenario. As such, just having 12 instead of 20 perturbed doses is often sufficient. Likewise, limiting the evaluation to only the critical OARs can lead to an even lower operation time.

5. Results and Discussion

In this chapter, the results of this study are presented. Overall the data of eight patients was examined, with the patients named BK001, BK002, BK003, BK004, BK006, BK007, BK010 and BK011. The results concerning the different margin concepts were examined with regard to target coverage and organ sparing. Due to the optimization to the CTV when using robust optimization, only the CTV coverage was assessed. As noted in chapter 4.2, Series 4 used a different target volume than Series 1-3. Therefore, when evaluating the target coverage, the CTV was examined for Series 1-3, while the GTV was used for Series 4. As Series 4 worked with the GTV, the summed plans are also evaluated based on the GTV. The robustness of the plans was determined by looking at the worst-case scenario under the influence of perturbances. Along with the fluctuation range, the direction of isocenter shifts that cause the highest changes in the dose-volume parameters were determined. For the purpose of readability, the robust plans with robust objectives solely to the CTV are referred to as 'RobustA'. The robust plans with additional robust objectives to the brainstem and chiasm are respectively denoted as 'RobustB'. The directions 'x', 'y' and 'z' refer to the axis in left-right, cranio-caudal and anterior-superior direction, respectively.

5.1. Plan recreation

The recreation of the original treatment plans used the standard 5mm margin expanding the CTV to the PTV, and had the primary goal of matching the plan quality of the treatment plans provided by the PSI. The corresponding DVHs for Series 1 of patient BK007 can be seen in figure 5.1, and their isodose curves in figure 5.2. It should be noted that the original treatment plans also calculated the dose outside of the body, while this is not the case for the plans made with RayStation, where by default the dose was only calculated within the external body structure. Minor differences between the plans could be observed, the RSL plan matched the original plan in target coverage while providing slightly better

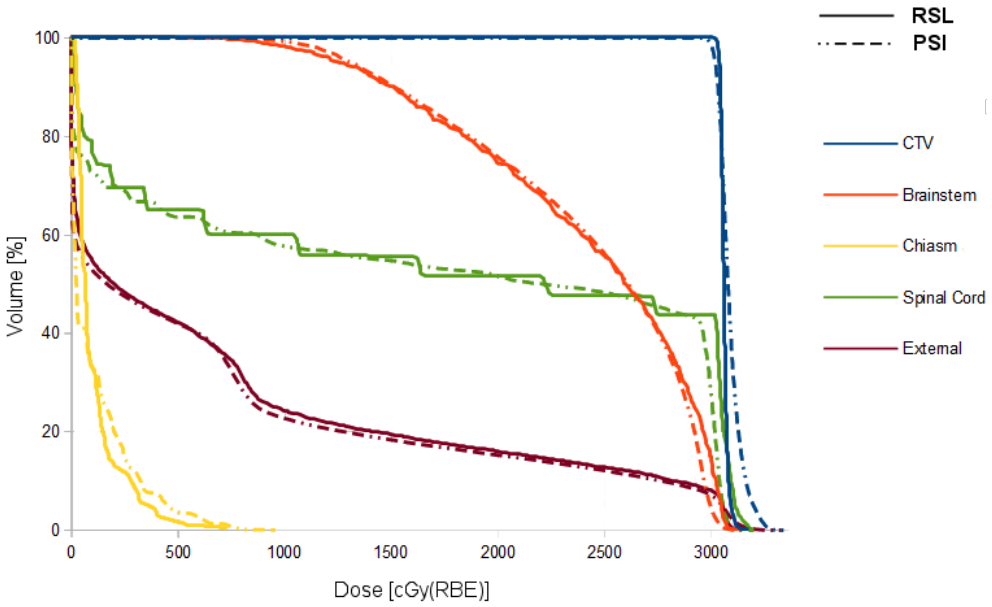

Figure 5.1.: DVH comparison between PSI and RSL treatment plans for Series 1 of BK007.

sparing for a few organs.

Overall, $D_{2\%}$ and $D_{98\%}$ of the CTV never deviated by more than 2.5% from the original plan considering all series, with the slightly higher deviations occuring in the patients BK004 and BK006. In most cases, such as in all Series 1 plans, the two plans deviated by less than 1% in $D_{2\%}$ and $D_{98\%}$. The higher deviations are found in the series that have lower presciption doses and more pronounced TechPTVs for brainstem and spinal cord sparing.

For the brainstem, $D_{2\%}$ usually equaled the prescription dose due to an overlap of the brainstem and the PTV while the mean dose was lower depending on how much of the brainstem was directly covered by the tumor. The mean dose and $D_{2\%}$ of the brainstem generally deviate at most 3% from the original plans, with a few outliers to up to 8% in Series 3 and 4 in cases where a less modulated TechPTV was chosen for the RSL plan. In exchange, the target coverage was enhanced in those cases. The $D_{2\%}$ of the spinal cord was generally close to the prescription dose in Series 1 and 2. Deviations for the spinal cord values went up to 7% in Series 1 and 2 and to higher percentages in Series 3 and 4. However, the higher deviation percentages were a result of low dose values (1-2 Gy (RBE)). For the chiasm, the

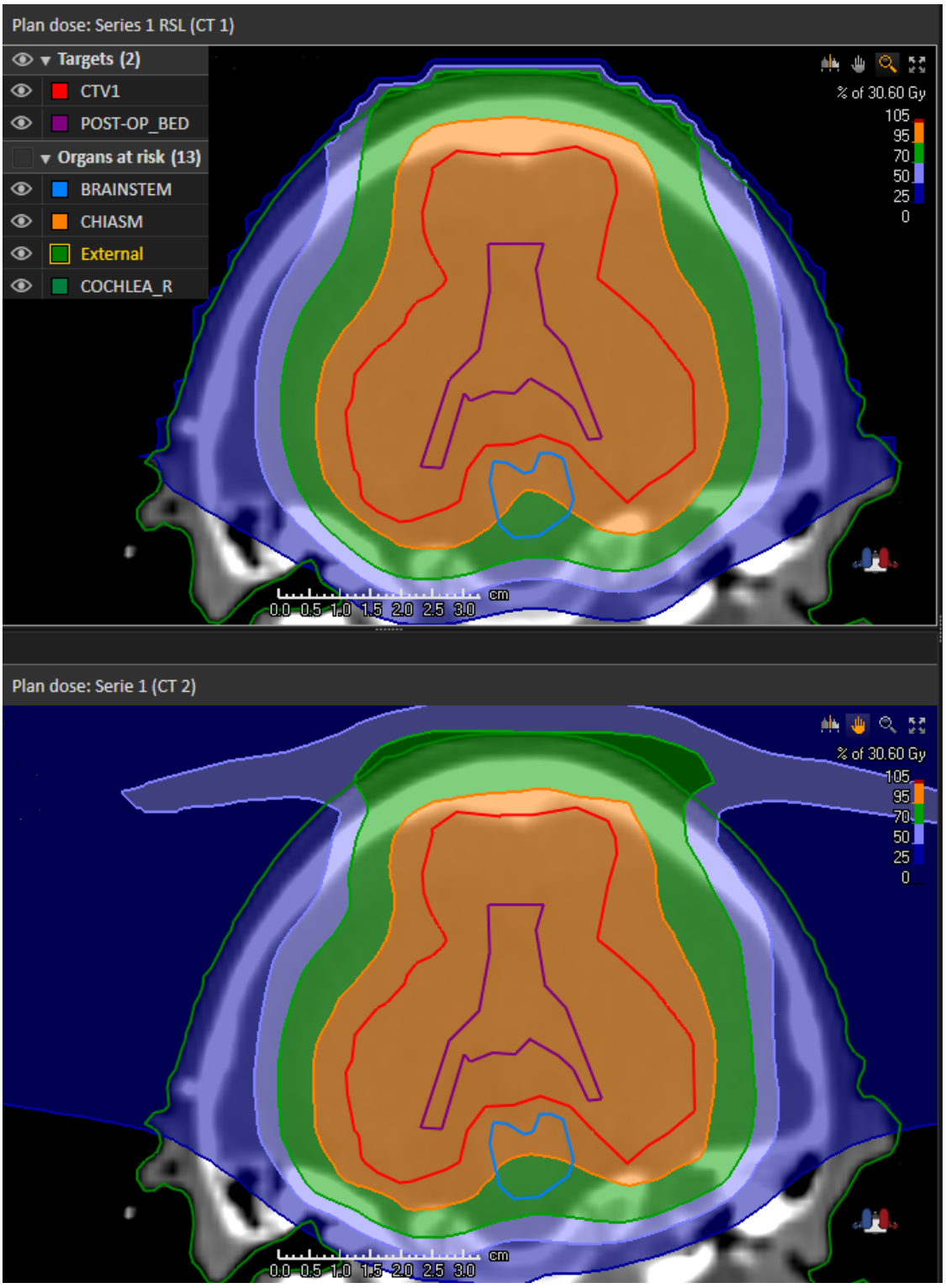

Figure 5.2.: Isodose comparison between PSI and RSL treatment plans for Series 1 of BK007.

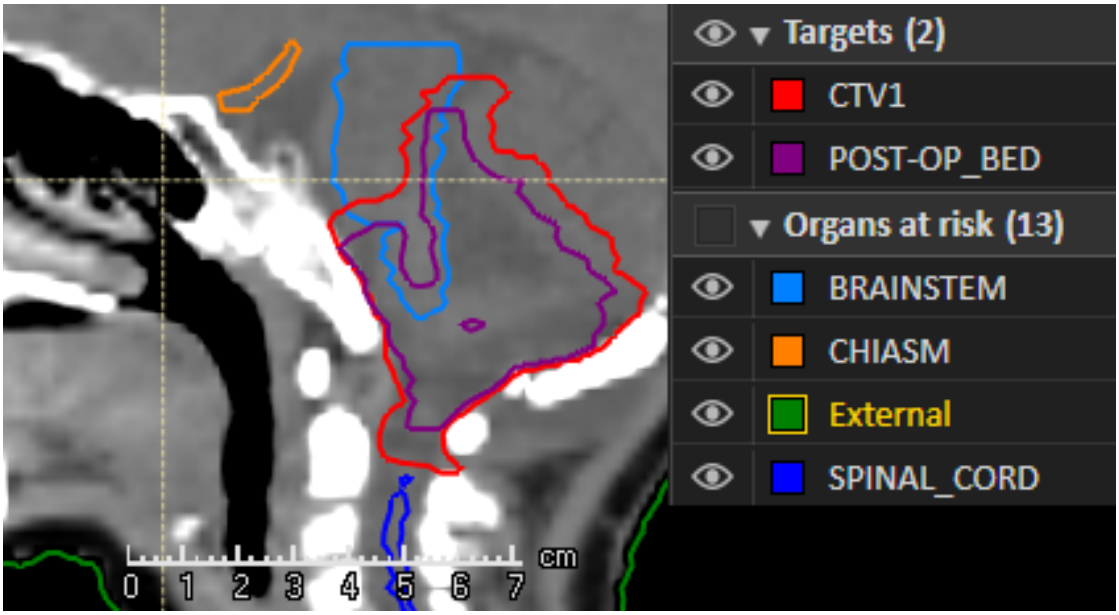

Figure 5.3.: Basic target volume and OAR outline of patient BK001.

values from the RSL plans were generally up to 5% lower, with higher percentages in Series 3 and 4. As such, it can be concluded that the recreation succeeded in matching the target coverage of the original plans. Moreover, no significant hot spots within the patients were observed, so that the assumption that $D_{2\%}$ can represent the dose maximum is correct.

5.2. Comparison of different margin concepts

The comparison of the different margin concepts was undertaken on the basis of two example patients, BK001 and BK007, which were selected to represent the patient collective as a whole, as they represented the two patient groups where the GTV coverage in the summed plan was slightly lower or higher for the robust plans. The respective anatomic situations of the patients can be seen in figures 5.3 and 5.4. Their differences in terms of tumor characteristics led to differences in the plan setup and the degree to which certain OARs are affected. For both chosen patients, the RSL plan was a good recreation of the original plan (see figure 5.2), with $D_{2\%}$ and $D_{98\%}$ of the CTV not deviating more than 1.5%. Both patients were evaluated regarding the nominal scenario as well as their robustness.

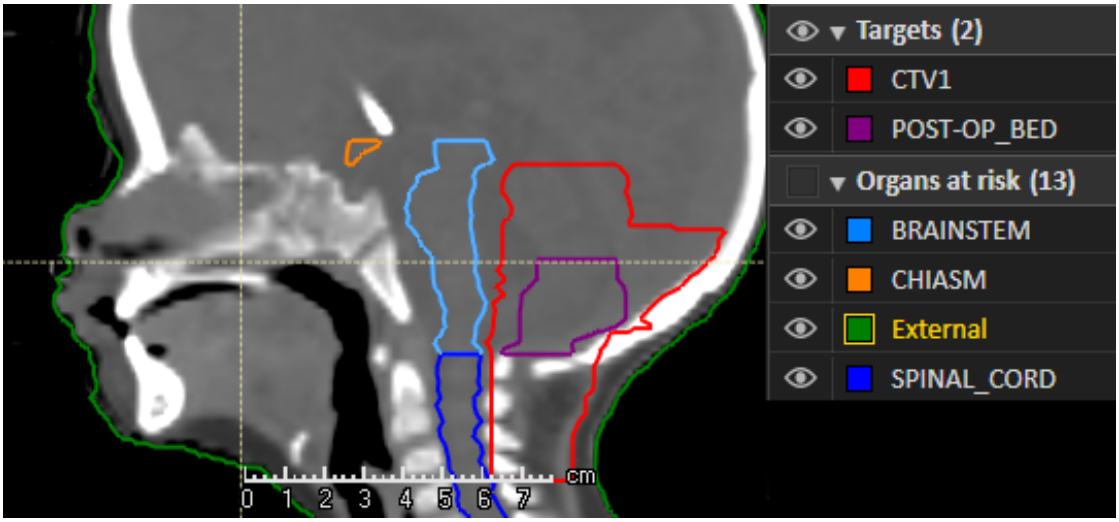

Figure 5.4.: Basic target volume and OAR outline of patient BK007.

For the nominal scenario, the calculated summed plans were most relevant, as they give information about the overall treatment quality of plans with alternative margin concepts. The robust evaluation was performed on basis of the individual series to obtain more detailed observations of the effect of the margins on the robustness. The OARs analyzed for both patients were the brainstem, spinal cord, chiasm and the external contour. Brainstem and spinal cord were evaluated as they are directly affected by the tumor, while the chiasm was chosen as a robust optimization target as outlined in chapter 4.3. The average dose of the 'External' ROI was examined to gain information about the overall dose which the body is exposed to. Additionally, the results for the hippocampus in patient 1 and the cochlea in patient 2 were analyzed as further examples of OARs not in close proximity to the tumor.

5.2.1. Patient BK001

Nominal scenario

The results from the summed plans for the first example patient are summarized in tables 5.1, 5.2 as well as 5.3. Figure 5.5 shows the DVH of the GTV and a few select OARs. The DVH shows that, if combined over all series, the different margin concepts maintained sufficient CTV coverage compared to the original approach

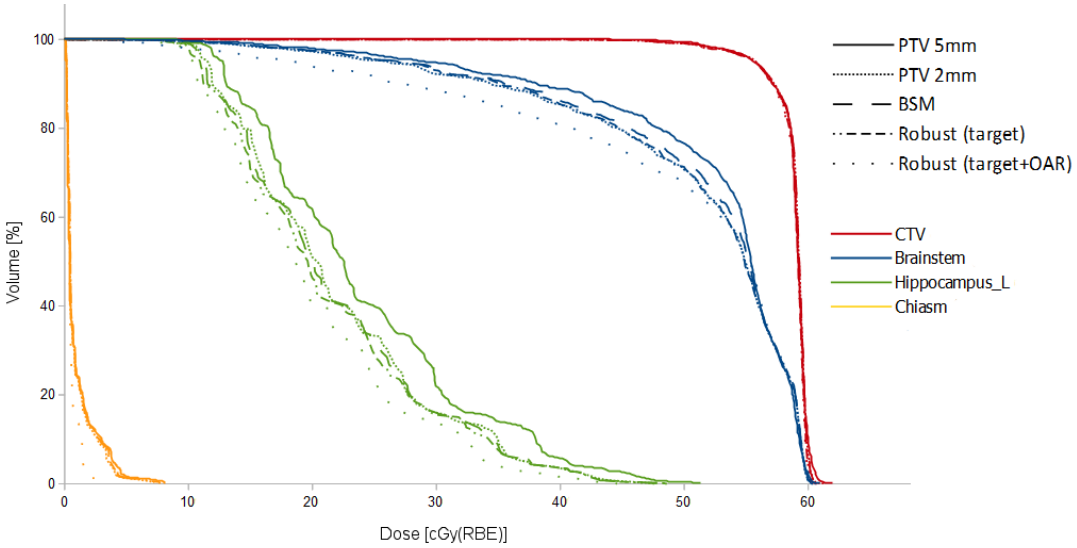

Figure 5.5.: DVH comparison between the different margin concepts for the summed plans of BK001.

of 5mm while lowering the dose to some OARs, most significantly for the hippocampi. The numbers show that the median dose $D_{50\%}$ fulfilled the prescription of 59.4 Gy (RBE) to the GTV within 0.5% for all margin concepts. The values for $D_{98\%}$ and $V_{95\%}$ were lower than in other patients due to the optimizations being carried out with a TechPTV that differed by more from the investigated CTV/GTV in Series 3 and 4. These values were highest for the RSL and BS plan, followed by the 2mm plan, while being lower by around 1.5% when applying robust optimization in either variant. The $D_{2\%}$ did not exceed the prescription dose by more than 2.5% in any nominal scenario and was highest for the RSL plan. The other four plans achieved marginally (around 1 Gy (RBE)) smaller doses. While the overall differences in term of CTV coverage were small and took place in ranges below 1 Gy (RBE), it still shows that the usage of robust optimization led to a slightly decreased CTV dose. Both the variant with and without additional objectives to OARs performed very similarly regarding the CTV.

For the brainstem (table 5.2), $D_{2\%}$ stayed nearly the same regardless of the margin concept, with all alternative plans leading to a value which was lower than that of the RSL plan by less than 0.5 Gy (RBE). As the brainstem was an OAR directly affected by the tumor, the $D_{2\%}$ of the brainstem reached values comparable to the $D_{2\%}$ of the CTV. The clinical brainstem constraint of 59.4 Gy (RBE) was exceeded by all plans by 0.5 - 1 Gy (RBE). The average dose to the brainstem however was influenced by the choice of margin concept. The RSL plan at 52 Gy (RBE) led to

Summed Plan	CTV				GTV			
Dosimetric Parameter	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$
	[Gy (RBE)]			[%]	[Gy (RBE)]			[%]
RSL	61.1	59.4	54.6	93.5	60.7	59.2	52.7	92.9
2mm	60.4	59.3	54.2	92.5	60.3	59.3	52.4	93.0
BS	60.3	59.3	54.2	92.6	60.2	59.3	52.7	93.0
RobustA	60.1	59.1	53.7	91.4	60.1	59.2	51.9	92.9
RobustB	60.0	59.1	53.7	91.3	60.0	59.2	51.9	92.5

Table 5.1.: Nominal CTV and GTV values of the summed plans from BK001.

Summed Plan	Brainstem		Chiasm		Spinal Cord		External
Nominal dose[Gy (RBE)]	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
RSL	60.1	52.0	4.6	1.0	42.9	13.0	8.5
2mm	59.8	50.7	4.1	0.9	41.6	12.0	8.0
BS	59.8	51.1	4.3	1.0	42.1	12.0	7.9
RobustA	59.8	50.8	4.2	1.0	41.5	11.9	7.6
RobustB	59.9	49.1	1.7	0.5	41.4	11.9	7.4

Table 5.2.: Nominal OAR values of the summed plans from BK001.

the highest value for the average dose. It was followed by the BS, RobustA and 2mm plans, which achieved values that were lower by 1-3 Gy (RBE). At a dose reduction of 3 Gy (RBE), the RobustB plan significantly outperformed the other plans in terms of brainstem sparing as it was included as a robust optimization objective.

The enhanced sparing for OARs receiving robust objectives could also be observed for the chiasm. Both the $D_{2\%}$ and the average dose of the chiasm showed a similar behaviour as the average dose of the brainstem. The RSL plan led to the highest value of $D_{2\%}$ at 4.6 Gy (RBE), followed by the BS, RobustA and 2mm plans, which achieved values lower by 6%, 9% and 11%, respectively. If choosing the chiasm as a robust objective, the resulting plan led to a $D_{2\%}$ of 1.7 Gy (RBE). Likewise, the values for the average chiasm dose behaved similarly, with the RSL plan at 1 Gy (RBE). Only the RobustB plan resulted in an average dose that was 45% lower. As the chiasm received low doses to to its distance to the tumor, pertur-

Summed Plan	HippocampusL		HippocampusR	
Nominal dose[Gy (RBE)]	$D_{2\%}$	Mean	$D_{2\%}$	Mean
RSL	45.8	24.0	37.5	19.2
2mm	42.1	21.7	34.5	17.5
BS	42.3	21.6	34.7	17.7
RobustA	41.8	21.2	33.7	17.2
RobustB	39.5	19.9	31.3	15.8

Table 5.3.: Additional OAR values of the summed plans from BK001.

bations led to deviations of over 100%. Using the chiasm as a robust objective ensured that the dose to the chiasm would not exceed the nominal value in the perturbed scenarios, leading to a high relative reduction of its dose parameters.

Of the left and right hippocampus (table 5.3), the left one received more dose due to its position in relation to the beams. The RSL plan led to the highest $D_{2\%}$ at 45.8 Gy (RBE). The BS, 2mm and RobustA plans achieved dose values at around 40 Gy (RBE), while the RobustB plan achieved a reduction of over 13% to 39.5 Gy (RBE). The highest average dose of 24 Gy (RBE) also resulted from the RSL plan, followed by the 2mm and BS plan which are lower by 9-10%. The RobustA plan performed similarly to those two margin concepts with a dose reduction of over 11%, while the RobustB plan achieved a reduction of over 17%. The results of the right hippocampus mostly mirrored those of the left hippocampus, with the RSL plan leading to the highest $D_{2\%}$ and mean dose at 37.5 and 19.2 Gy (RBE). As before, the RobustB plan led to the lowest doses at 31.3 and 15.8 Gy (RBE). Thus, it can be seen that the hippocampi profited from the additional robust objectives despite not being directly used as a robust optimization objective.

In case of the spinal cord, the differences between the margin concepts were not that extreme. The highest $D_{2\%}$ of 43 Gy (RBE) resulted from the use of 5mm margins, while the other plans' doses were up to 1.5 Gy (RBE) lower. In a similar manner, the highest average dose of 13 Gy (RBE) belonged to the RSL plan, while the other margins led to around 12 Gy (RBE). Even when compared to OARs that were not chosen as robust objectives, such as the hippocampus, the spinal cord profited slightly less from alternative margin concepts. This is mostly due to the treatment approach, where the Series 1 plans included measures for symmetrical bone irradiation, which makes the 5mm, beam-specific and 2mm margins more

Series 1, CTV, $D_{98\%}$				
Margin	nominal[Gy (RBE)]	worst case[Gy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	30.1	29.7	z: 0.2; 3.5	z: 0.2; -3.5
2mm	30	29.3	z: 0.2; 3.5	z: 0.2; -3.5
BS	30	29.6	z: 0.2; -3.5	z: 0.2; 3.5
RobustA	29.6	29	z: 0.2; 3.5	x: 0.2; 3.5
RobustB	29.6	29	z: 0.2; 3.5	x: 0.2; 3.5

Table 5.4.: Worst case scenarios of the $D_{98\%}$ of the CTV.

similar to each other. Moreover, Series 3 and 4 introduced additional spinal cord sparing by cutting off the CTV below the first vertebrae of the spinal cord. This cut-off was the same for all margin concepts including the robust plans, therefore slightly reducing the difference between them. The performance of the two different robust variants was also very similar, meaning that the spinal cord did not profit from the additional robust objectives.

The average dose to the External ROI was highest for the RSL plan at 8.5 Gy (RBE), followed by the 2mm, BS, RobustA and RobustB plans, which showed dose reductions of 6-13%. The overall gain when using the robust approach with robust objectives to OARs instead of the original 5mm margins was a reduction of the average dose by over 1 Gy (RBE).

Robust Evaluation

Series 1

Series 1 applied a prescription dose of 30.6 Gy (RBE) to a PTV expanded for symmetrical bone irradiation. The results for Series 1 of this patient are listed in the appendix, providing detailed data about CTV coverage and OAR sparing in perturbation scenarios. They show that, for all plans and scenarios, the median dose $D_{50\%}$ to the CTV fulfilled the prescription dose within a range of 0.5%. The $D_{2\%}$, which was highest for the RSL plan and lowest for the robust approaches, was subject to deviations of less than 1% for all margin concepts. The perturbation scenario of a 0.2 cm shift in anterior-posterior direction with +3.5% density perturbation was responsible for the highest $D_{2\%}$ regardless of margin concept. Nominal $D_{98\%}$ values and their worst case scenarios are listed in table 5.4. It can be seen that the target coverage was similar for all plans. Although the worst

case scenario was the same for both robust approaches as for the RSL and the 2mm plan, the robust approaches were influenced less by the isocenter shift and more by the range errors. As also seen in detail in the appendix, the three worst case scenarios featured the same isocenter shift when using a non-robust margin. Overall, target coverage for the CTV was given while dose hotspots were avoided. The slightly lower $D_{98\%}$ of the robust can be explained by them being the only plans that did not use a PTV, which has been expanded to guarantee symmetrical bone sparing.

For the brainstem, the nominal $D_{2\%}$ was within 1% for all plans, with the value for the RSL plan being the highest. All deviations stemming from the perturbed scenarions were below 1% as well. The $D_{2\%}$ of the RobustB plan was minimally higher than that of the RobustA plan. However, it succeeded in lowering the average brainstem dose below that of the 2mm, BS and RobustA plans, which in turn led to a lower dose than the RSL plan by 10-14%. To note is that the scenarios that lead to the highest average doses were the same for all margin concepts, namely the +0.2 cm isocenter shift with -3.5% density perturbation.

The nominal dose value for the $D_{2\%}$ of the chiasm amounted to 2.5 Gy (RBE) in the first series when using the RSL plan, with the values of the 2mm, BS and RobustA plan being minimally lower. Only the RobustB plan led to a dose that was lower by over 50%. The relative deviations under perturbations amounted to around 200% regardless of the margin concept. Those high relative fluctuations were a result of the low initial values, as the absolute fluctuation ranges were not unusual for an OAR further away from the tumor location. Due to the lower nominal chiasm dose, the absolute range of $D_{2\%}$ values was only 2.5 Gy (RBE) for the RobustB plan, as opposed to around 5 Gy (RBE) in the other plans of this patient and series. The behavior of the average chiasm dose was the same, with the RobustB plan leading to a over 50% lower nominal dose value and deviation range under perturbations. While the RobustB plan performed significantly better for the chiasm, it has to be kept in mind that the involved dose values were low and far below its clinical threshold.

To gain information about an OAR that was exposed to a higher dose level without being the or right next to the tumor location, the results for the hippocampus were examined. The nominal $D_{2\%}$ of both the left and right hippocampus were highest for the RSL plan at 27.7 and 24.2 Gy (RBE), followed by the BS and RobustA plan which perform similarly. The lowest dose was achieved by the RobustB plan at 23.7 and 18.9 Gy (RBE). The fluctuation ranges for the $D_{2\%}$ of the left hippocampus were up to $\pm$3.5 Gy (RBE) for all margin concepts, with the

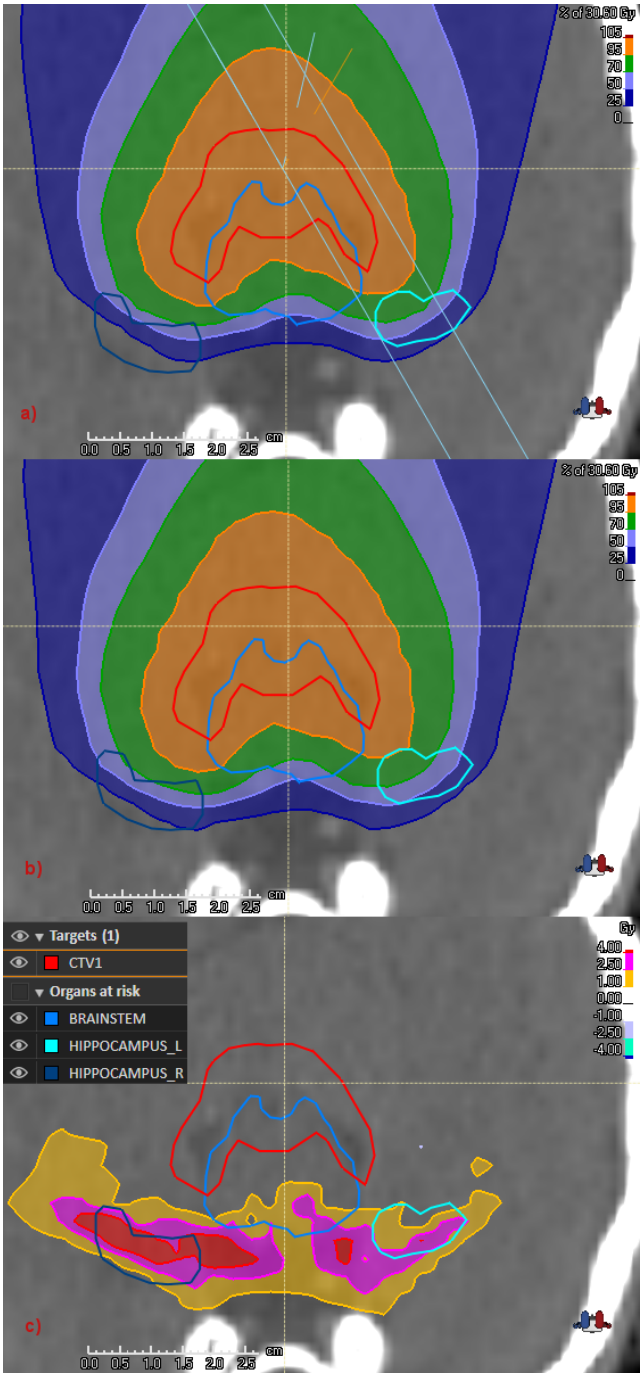

Figure 5.6.: Comparison between the a) nominal and b) perturbed (z = 0.2 cm, d= -3.5%) scenario of the RSL plan for patient BK001, Series 1. c) Dose difference map showing the additional dose to the hippocampi in the perturbed case.

lowest absolute range belonging to the RobustB plan. The average dose for the left hippocampus fluctuated in a range of 5.5 to 6 Gy (RBE), with the RSL plan resulting in both the highest deviation and highest nominal value. For all margin concepts, overestimating the density by 3.5% led to significantly higher dose values as the beams traverses more tissue than anticipating. Figure 5.6 shows the location of the hippocampus in relation to the tumor and the proton beams, illustrating that effect. While the range error had the biggest influence on the result, it can also be seen that shifts the isocenter by 0.2 cm in x- or z-direction moved the beam responsible for most of the dose towards the hippocampus, leading to higher perturbed doses. As such, the worst case scenario for the hippocampus resulted from a shift of 0.2 cm in z-direction, and the second worst case scenario came from a shift in x-direction, both while overestimating the density. The additional dose in the worst case scenario when applying the 5mm margin can be seen in figure 5.6. As comparison, figure 5.7 illustrates the difference between the nominal and the worst case scenario for the RobustB plan. It can be seen how the robust plan led to slightly less additional dose in the worst case. While the difference between margin concepts was not as significant as for the chiasm, based on the hippocampus it could be shown that even organs that are not directly used as robust objectives can profit from them.

The $D_{2\%}$ of the spinal cord was in the nominal scenario highest for the RSL at 28.9 Gy (RBE) and lowest for the 2mm plan at 28.4 Gy (RBE). The differences in fluctuation were minimal, with a range of around ± 1.5 Gy (RBE) for all margin concepts. In regards to the average dose, the most noticeable difference was the higher overall dose resulting from the RSL plan. The corresponding deviation under perturbances amounted to around 35%, or 3 Gy (RBE), for all margin concepts. Compared to other OARs, the spinal cord results were the least affected by the choice of margin, which is partly owed to the measures that were taken to ensure symmetrical bone irradiation and thereby were partly equal to the actual margins.

Series 2

Series 2 applied a prescription of 19.8 Gy (RBE) to the same PTV as in Series 1, however without additional margin to ensure symmetrical bone irradiation. Its results are listed in the appendix. They show that the $D_{50\%}$ of the CTV fulfilled the prescription dose within a range of 0.6% for all scenarios. The $D_{2\%}$ is illustrated in figure 5.8 for all margin concepts in form of a box and whiskers plot. The RSL plan led to the highest dose values at around 20.5 Gy (RBE), while the robust

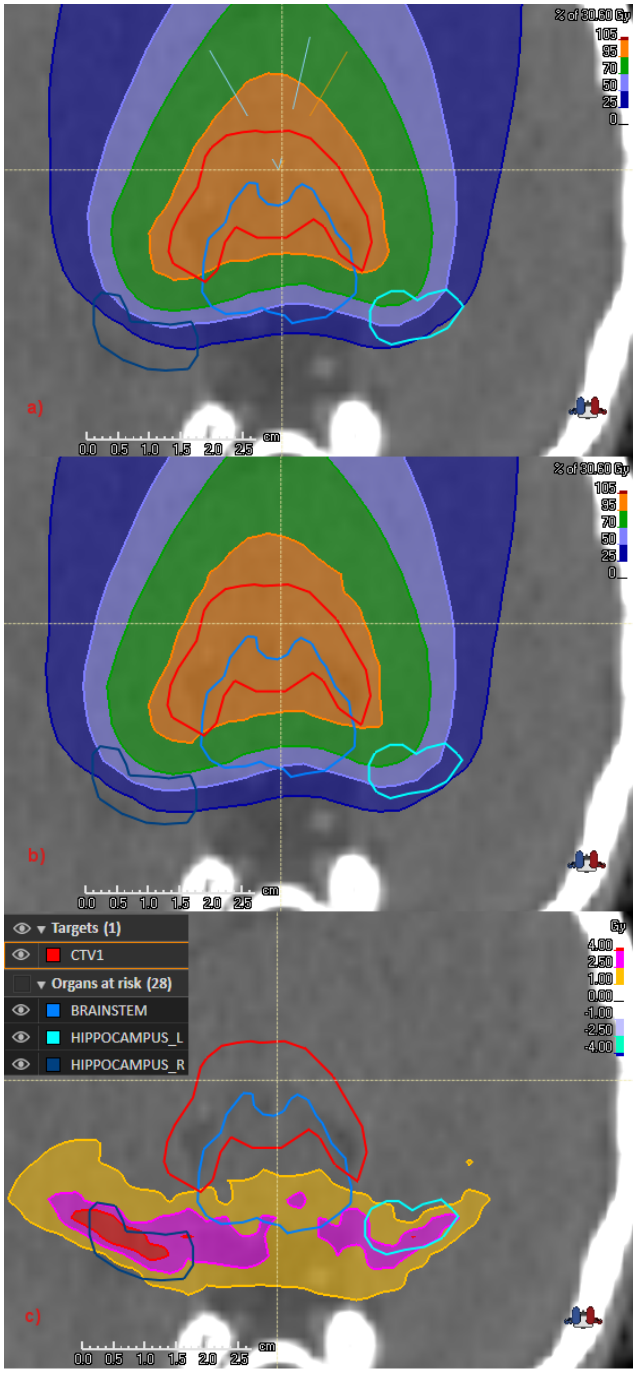

Figure 5.7.: Comparison between the a) nominal and b) perturbed (z = 0.2 cm, d= -3.5%) scenario of the RobustB plan for patient BK001, Series 1. c) Dose difference map showing the additional dose to the hippocampi in the perturbed case.

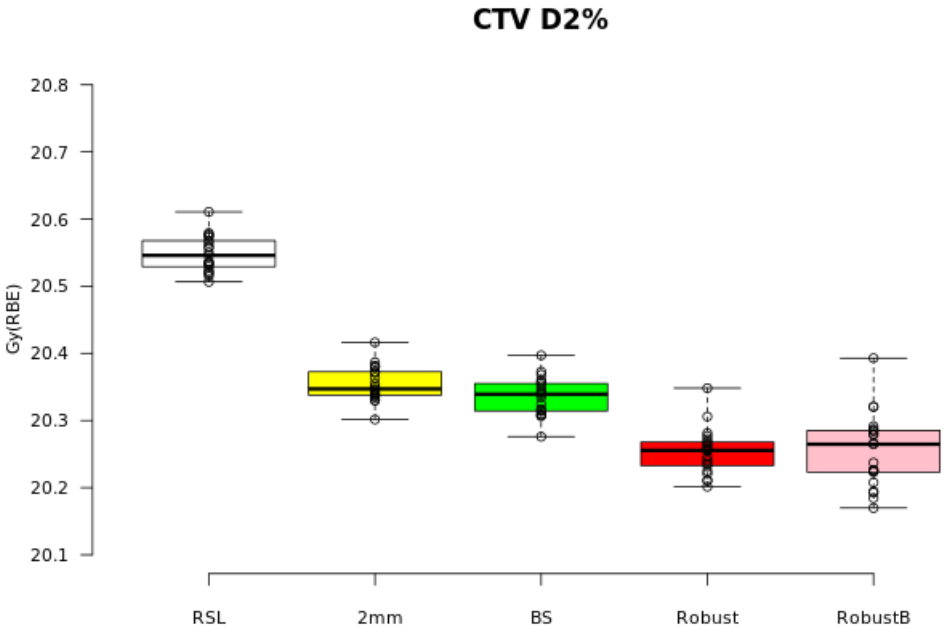

Figure 5.8.: Box and Whiskers plot of the $D_{2\%}$ of the CTV. (BK001, Series 2)

approaches achieved the lowest ones at 20.3 Gy (RBE). The target coverage as described by the $D_{98\%}$ is shown in figure 5.9. In the nominal case, the RSL plan resulted in the highest value. The $D_{98\%}$ of the robust approaches led to nominal values that were over 0.5 Gy (RBE) lower than that of the RSL plan. The CTV coverage was still acceptable in the nominal cases, but in even in the RSL plan, the worst case scenario led to a $D_{98\%}$ under 95% of the prescription dose. For the other margin concepts, those values even approached 90% of the prescription dose. When comparing RobustA to RobustB, it can be seen that the robust objective to the brainstem did influence the CTV coverage, leading to a slightly higher fluctuation range due to the conflict between sparing the brainstem and securing CTV coverage. As the CTV coverage for this series was specifically hard to reach, this would be one of the cases where the 5mm margin of the RSL plan might be most appropiate to ensure that the $D_{98\%}$ stays above 95%.

Concerning the brainstem itself, the nominal $D_{2\%}$ was basically the same regardless of the margin concept, with up to 1% deviation range. Similar deviation ranges applied to the mean brainstem dose as well, with the nominal value being the lowest for the RobustB plan. The worst case scenario of the RobustB plan still led to a lower average brainstem dose than the nominal scenario of the RSL plan. The brainstem in general profited from the usage of robust objectives, as the $D_{2\%}$ did

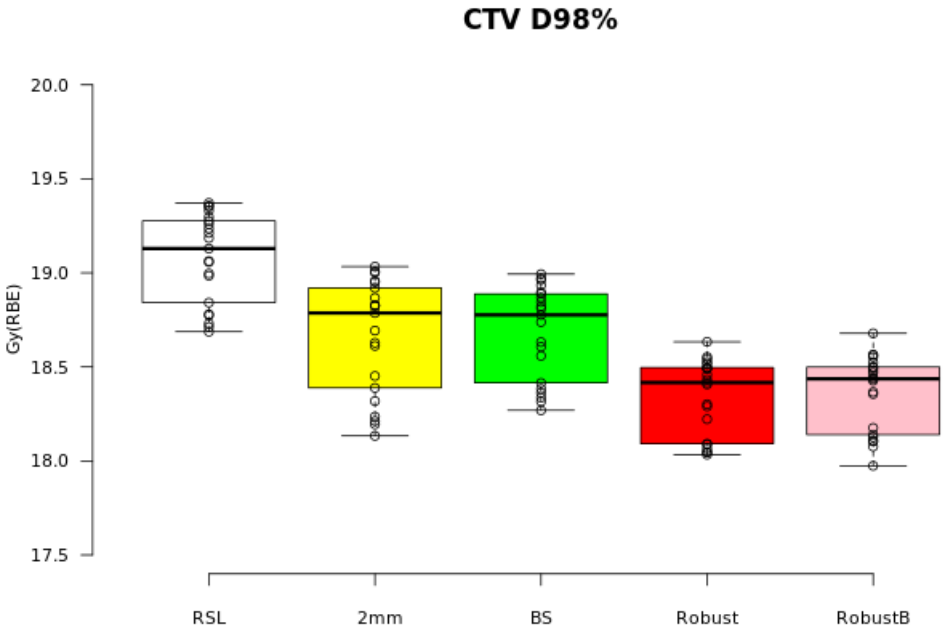

Figure 5.9.: Box and Whiskers plot of the $D_{98\%}$ of the CTV. (BK001, Series 2)

not change significantly between the different margin concepts, while the average dose was lowered.

The chiasm, as the other OAR that was used as robust objective, likewise profited from the corresponding RobustB approach. The chiasm was only exposed to low dose levels and is located in an area that was unlikely to be severely affected by the changes made to the PTV between Series 1 and Series 2. In the nominal case, the BS, 2mm and RobustA plan led to a slightly lower $D_{2\%}$ and average dose compared to the RSL plan. The RobustB plan however led to doses that were lower by 1.8 and 0.4 Gy (RBE), respectively. This improvement was due to the fact that further optimization of the chiasm did not conflict significantly with other goals. Thus, it was possible to ensure that any perturbed scenario of the RobustB plan did not lead to doses higher than the nominal doses of the other plans. This was the optimal result that comes from changing a non-robust objective to a robust objective. This also led to significantly lower deviation ranges.

For both hippocampi, the nominal $D_{2\%}$ was highest for the RSL plan, followed by the BS, the 2mm, the RobustA and the RobustB plan. For all margin concepts, the deviation range was around ±3 Gy (RBE), which amounted to 40-50% of the

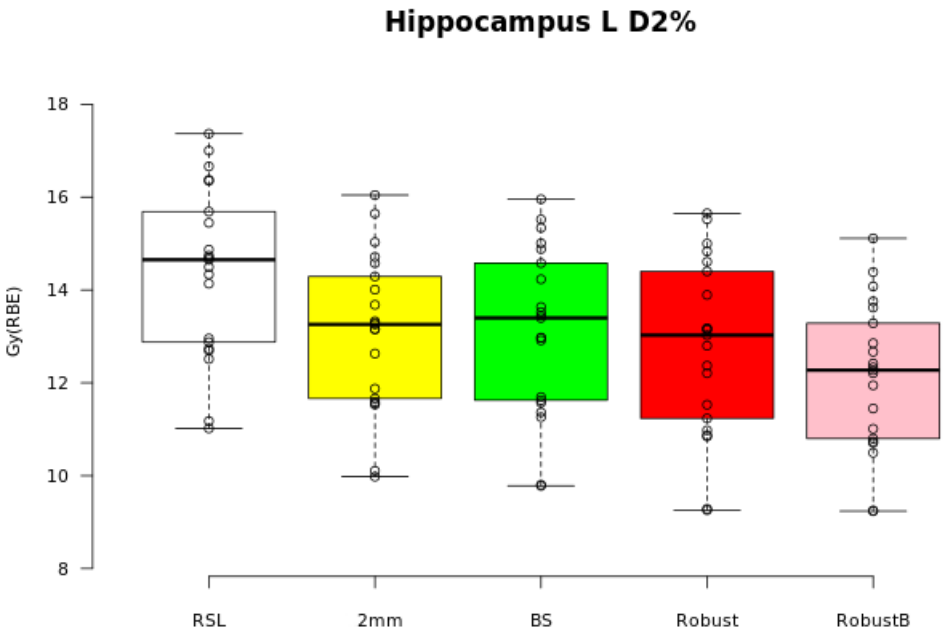

Figure 5.10.: Box and Whiskers plot of the $D_{2\%}$ of the left hippocampus. (BK001, Series 2)

nominal value depending on the margin concept. As an example, the boxplot of $D_{2\%}$ of the left hippocampus is depicted in figure 5.10. As was the case for Series 1, overestimating the density led to the highest dose values compared to the perturbed scenarios that correctly or underestimate the density. This applied in general to the dose values of all OARs for both Series 1 and 2. Exceptions were the spinal cord in Series 1, which is an organ which is not located mostly behind the tumor from the beams' eye views; and the $D_{2\%}$ of the brainstem which barely differed between the margin concepts due to being heavily correlated to the CTV coverage.

The spinal cord was the OAR where the most differences concerning the nominal values to the Series 1 results were expected, as it was influenced most by the symmetrical bone irradiation. Whereas the dose values of the alternative margin concepts were fairly similar to that of the RSL plan, the differences were more pronounced in Series 2. The non-RSL plans showed a nominal $D_{2\%}$ that was lower by 5-10% compared to the RSL value of 28.9 Gy (RBE). The corresponding fluctuation ranges of the $D_{2\%}$ were ± 2.5 Gy (RBE) for the RSL and robust approaches and ± 3 Gy (RBE) for the 2mm and BS plan. In comparison to Series 1, this made

the spinal cord results more similar to the results of other OARs, where reduction of the used margin led to lower dose values.

Series 3

Series 3 differed from Series 1-2 in that a part of the CTV/PTV was cut off to spare the spinal cord. While the CTV for the robust approaches was also cut off at the same line, the use of robust optimization basically introduced a margin where the RSL, BS and 2mm plans use none, leading to the expectation of slightly higher spinal cord values. Moreover, the CTV dose values that were extracted from the plans refer to the full CTV without the cut-out, making the values for $D_{98\%}$ and $V_{95\%}$ of the CTV not very significant in terms of determining the target coverage by comparing them to typical values which constitute an appropiate coverage. However, they could still be used to compare the difference margin concepts.

Results show that the $D_{50\%}$ of the CTV fulfilled the prescription dose within a range of 0.7% for all plans and scenarios. The nominal values and values of the worst case scenarios are listed in table 5.5. While the dose values showed the same tendencies as in Series 1 and 2, thus serving as further confirmation of that behaviour, the absolute numbers were in the dimension of a few cGy (RBE). Likewise, the scenario of a 0.2 cm shift in anterior-posterior direction with +3.5% density perturbation, which was responsible for the worst case scenarios in Series 1 or 2, also led to the highest $D_{2\%}$ for all margin concepts except the 2mm margin, where it was responsible for the second highest dose. The $D_{98\%}$ was 2.2-2.3 Gy (RBE) for the margin concepts, being highest for the RobustB plan. The RobustA plan led to a $D_{98\%}$ that was higher by 0.9%, while the BS and 2mm margin were lower by 1.4% and 2.7%, respectively. While the absolute numbers are small, the relative differences were in the same magnitude as those of the former Series. The slightly higher $D_{98\%}$ values in Series 3 in the robust approaches are in contrast to the results of Series 1 and 2. This can be explained with the CTV cut-off which was used for spinal cord sparing, as this equals a small area where a margin of 0 mm was used for the 2mm, BS and RSL plan.

The nominal $D_{2\%}$ of the brainstem was comparable for all margin concepts at 3.7 Gy (RBE). The fluctuation range was highest for the RobustA plan at ±0.5% and lowest for the 2mm and RSL plan at below ±0.2%, keeping in line with the observed consistency in brainstem $D_{2\%}$ values in the first two series. For the brainstem average, it could be observed that the 2mm, BS and RobustA plan all led to a slightly lower value than the RSL plan at a 1-2% lower dose, while the

Series 3, CTV, $D_{2\%}$				
Margin	nominal[cGy (RBE)]	worst case[cGy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	371.5	373.6	z: 0.2; 3.5	z: 0.2; -3.5
2mm	367.8	369.1	y: 0.2; 3.5	z: 0.2; 3.5
BS	367.6	368.9	z: 0.2; 3.5	y: 0.2; 3.5
RobustA	366.8	368.2	z: 0.2; 3.5	y: 0.2; 3.5
RobustB	366.6	368.9	z: 0.2; 3.5	y: 0.2; 3.5

Table 5.5.: Worst case scenarios of the $D_{2\%}$ of the CTV. Dose values in cGy (RBE) to better show the differences.

RobustB plan led to a 5% reduction. None of the margin concepts led to high deviations under perturbation for the mean dose.

As the $D_{2\%}$ and average dose of the chiasm were in the dimension of cGy (RBE), their absolute values are of little practical relevance. However, the same tendencies and similar relative dose reductions can be seen when applying the RobustB plan, which lowered the nominal $D_{2\%}$ by 55% and the nominal mean dose by 33% compared to the RSL plan.

For both hippocampi, the RSL plan led to the highest nominal $D_{2\%}$ and average dose. In case of the left hippocampus, the 2mm, BS and RobustA plans achieved a 10% lower $D_{2\%}$ and average dose. The RobustB plan furthermore profited from the additional robust objectives and a dose reduction of around 15% for both values. In regards to the right hippocampus, the $D_{2\%}$ was reduced by 3.5% for the BS and RobustA plan, while the 2mm value was lower by 7%. In comparison, the RobustB plan achieved a 15% reduction of $D_{2\%}$. The highest average dose of the RSL plan was followed by the BS, 2mm, RobustA and RobustB plan at 5.5%, 7%, 9% and 15% lower doses, respectively. Noticeable was the lower average but higher $D_{2\%}$ dose of the RobustA plan when compared to the 2mm plan, which suggests that that the average dose profited from the overall lower dose throughout the body which stems from using a robust approach. However, the part of the hippocampus that intersects with a beam path still was exposed to a higher maximum dose due to the robust margin having a stronger effect than the 2mm non-robust margin.

The spinal cord values confirmed the expectations that the robust approaches led to higher values of $D_{2\%}$ and the average dose due to the other margin concepts profiting from the PTV cut-off. Both robust approaches led to dose values that were higher by over 5% compared to the nominal RSL plan. There was no significant difference in the fluctuation ranges between the margin concepts, staying at 0.5 Gy (RBE) and 0.1 Gy (RBE) for the $D_{2\%}$ and average dose, respectively.

Series 4, Brainstem, $D_{2\%}$				
Margin	nominal[cGy (RBE)]	worst case[cGy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	546.4	550.7	z: 0.2; 3.5	y: -0.2; 3.5
2mm	545.5	549.1	x: 0.2; 3.5	z: 0.2; 3.5
BS	546.3	550.4	x: 0.2; 3.5	z: 0.2; 3.5
RobustA	547.5	549.1	x: -0.2; 0	y: -0.2; 0
RobustB	548.2	550.5	x: -0.2; 0	z: 0.2; 3.5

Table 5.6.: Worst case scenarios of the $D_{2\%}$ of the Brainstem. Dose values in cGy (RBE) to better show the differences.

Series 4

Series 4 was used as a boost and aimed at a different CTV/PTV than the first three series, targeting a subvolume (generally the GTV) of it to ensure that the tumor bed receives additional dose. As is the case in Series 3, particular care was given towards sparing the spinal cord, using the same cutoff below the first vertebrae.

The $D_{50\%}$ of the GTV fulfilled the prescription dose of 5.4 Gy (RBE) within 1% for all plans and scenarios. The nominal $D_{2\%}$ was nearly equal for all margin concepts, with differences under 0.1 Gy (RBE). Under perturbations, the RSL plan showed the lowest fluctuation ranges of $\pm 0.4\%$, while the robust approaches led to the highest ones at around $\pm 0.7\%$ for both approaches. The RSL plan also achieved the highest value of $D_{98\%}$, with the two robust approaches leading to values less than 1% below that. Meanwhile, the 2mm and BS plan resulted in a $D_{98\%}$ that was lower by about 5%, reinforcing the idea that the robust approaches performed better than the 2mm and BS plans in terms of CTV coverage in cases where the margin is not applied around the entire CTV due to for example the spinal cord sparing.

In the nominal scenario, the $D_{2\%}$ of the brainstem did not differ much between the different plans in this series either. As seen in table 5.6, the robust approaches lead to a slightly higher nominal dose, but basically the same worst case scenario as the RSL plan. The average brainstem dose was highest for the RSL plan, followed by the RobustA and RobustB plans, whose nominal values were lower by 0.8% and 1.8%. In comparison, the 2mm and BS plan led to a value that are lower by 2.5%. As the brainstem values were generally correlated with the CTV values, this likely had the same cause.

Left Hippocampus, RSL, $D_{2\%}$				
Series	nominal[Gy (RBE)]	worst case[Gy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
Series 1	27.7	30	z: 0.2; -3.5	x: 0.2; -3.5
Series 2	14.7	17.4	z: 0.2; -3.5	x: 0.2; -3.5
Series 3	2.6	3.1	z: 0.2; -3.5	x: 0.2; -3.5
Series 4	2.4	2.9	z: 0.2; -3.5	x: 0.2; -3.5

Table 5.7.: Worst case scenarios regarding the left hippocampus when using the original 5mm margin.

Left Hippocampus, RobustB, $D_{2\%}$				
Series	nominal[Gy (RBE)]	worst case[Gy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
Series 1	23.7	26.7	z: 0.2; -3.5	x: 0.2; -3.5
Series 2	12.2	15.1	z: 0.2; -3.5	x: 0.2; -3.5
Series 3	2.3	2.8	z: 0.2; -3.5	x: 0.2; -3.5
Series 4	1.1	1.4	z: 0.2; -3.5	x: 0.2; -3.5

Table 5.8.: Worst case scenarios regarding the left hippocampus when applying robust optimization with additional OAR objectives.

The values for the chiasm were even lower than in Series 3 due to the different beam angles, resulting in them being irradiated less despite the additional fraction. However, despite the order of magnitude being cGy (RBE), the RobustB plan still led to $D_{2\%}$ and an average dose that were lower by over 30% when compared to the RSL plan, with the accompanying reduced absolute fluctuation range.

Very noticeable is that at 2.4 and 0.8 Gy (RBE), the $D_{2\%}$ and mean dose of the left hippocampus were significantly higher for the RSL plan. The nominal $D_{2\%}$ of the other margin concepts was lower by 42-52%, respectively, while the nominal average dose was lower by 41-48%. Those comparatively high dose reductions occured due to the beam angles, as the left hippocampus was located on the edge of one beam path. Thus, the simple reduction of margins led to those high dose reductions. The right hippocampus showed results more comparable to those seen in previous series. The RSL plan still led to the highest and the robust approaches to the lowest values, but at 15% for the $D_{2\%}$ and 15-20% for the mean dose, the difference was not quite as large. Tables 5.7 and 5.8 show how the worst case scenarios of the hippocampus were the same regardless of the series. It was being particularly susceptible to overestimation of the density, as it was located behind the target volume and a lower density thus led to more dose reaching the hippocampii.

5.2.2. Patient BK007

Nominal scenario

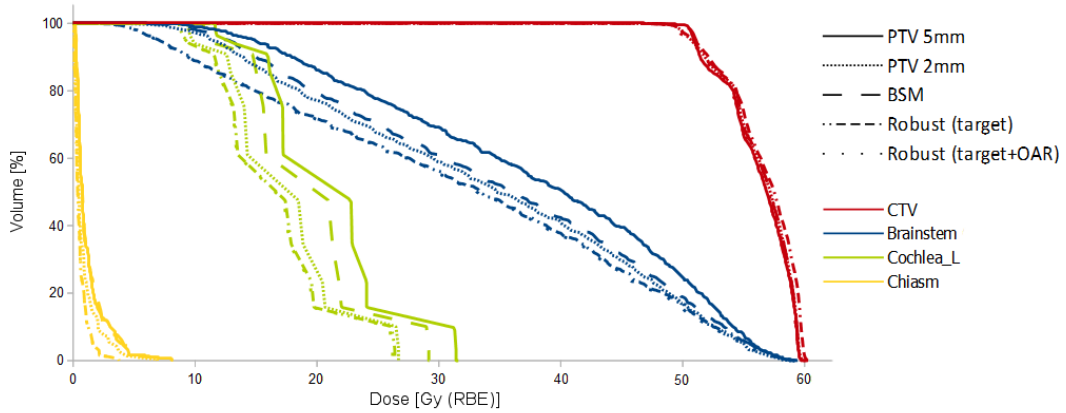

Figure 5.11.: DVH comparison between the different margin concepts for the summed plans of BK007.

Tables 5.9, 5.10 and 5.11 show the results of the summed plans for the different margin concepts in the nominal scenario for patient BK007. The DVHs for the CTV, brainstem, chiasm and the left cochlea are illustrated in figure 5.11, where the increased OAR sparing for the alternative margin concepts can be seen. Furthermore, it shows how the two different robust approaches performed the same even for the brainstem and chiasm.

All plans showed clinically acceptable target coverage for the GTV, with $D_{98\%}$ being above 99% of the prescription dose and $V_{95\%}$ being above 98% in all plans. The median dose $D_{50\%}$ fulfilled the prescription dose of 59.4 Gy (RBE) to the GTV within a range of less than 0.5% for all plans, with RobustA showing the highest deviation of nearly +0.5%. The $D_{2\%}$ of the GTV was within 0.1% of the RSL value for all plans except for RobustA, which led to a 0.65% higher value. Overall, the differences in GTV coverage were minor, with the notable tendency of the RobustA plan leading to the highest dose values. This suggests that the robust objectives for the GTV led to slightly higher doses, which were offset by the additional brainstem objective in the RobustB plan.

When looking at the OAR sparing of the brainstem, it can be seen that the $D_{2\%}$ was lower than in the RSL plan for all margin concepts except RobustA, which was

Summed Plan	CTV				GTV			
Dosimetric Parameter	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$
	[Gy (RBE)]			[%]	[Gy (RBE)]			[%]
RSL	59.6	56.9	50.6	55.2	59.7	59.4	58.8	100.0
2mm	59.6	57.2	49.9	57.9	59.7	59.4	58.9	100.0
BS	59.6	57.2	50.7	57.6	59.7	59.5	59.2	100.0
RobustA	60.0	57.5	49.9	59.7	60.1	59.7	59.4	100.0
RobustB	59.5	57.0	49.5	55.3	59.7	59.3	59.0	100.0

Table 5.9.: CTV and GTV values of the summed plans from BK007.

higher by 0.2%. The beam-specific plan and RobustB plan led to a $D_{2\%}$ lower by 0.3 Gy (RBE), while the 2mm plan resulted in the lowest value being 0.6 Gy (RBE) less than the RSL value. For the average brainstem dose, all alternative margin concepts led to a lower value than the RSL plan by 10-15%. The RobustB value was the lowest, showing the influence of the additional robust optimization objective to the brainstem.

For the chiasm, it has to be noted that it was not directly in a beam path or particularly close to the tumor, consequently it received doses of around 4-5 Gy (RBE) at most. The highest value for $D_{2\%}$ occured when using the beam-specific margins, followed by the RSL and the 2mm margins. The two robust approaches led to a $D_{2\%}$ which was lower by more than 2 Gy (RBE). As for the average dose, the RSL plan resulted in the highest value, with the beam-specific plan performing nearly the same. The 2mm plan led to around 30% less average dose, and the two robust approaches to 50% less dose than the RSL plan. For both $D_{2\%}$ and the average dose, the RobustB plan with the additional robust objective to the chiasm led to minimally lower values than the RobustA plan.

The lowest $D_{2\%}$ for the spinal cord was achieved by the 2mm plan at 52.7 Gy (RBE). Except for the BS plan, the other margin concepts led to values higher by less than 1 Gy (RBE). The beam-specific margin, which was not completely based on the TechPTV used for the RSL plan, resulted in a 1.5 Gy (RBE) higher $D_{2\%}$. For the average dose, the beam-specific plan again had the highest value at 25.2 Gy (RBE), followed by the RSL and the 2mm plan. The two robust approached lead to an average dose that was lower by around 10%. Thus, while the robust plans did not succeed in lowering the $D_{2\%}$ due to the proximity of the CTV, they still resulted in lower average doses.

Summed Plan	Brainstem		Chiasm		Spinal Cord		External
Nominal dose[Gy (RBE)]	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
RSL	57.2	37.9	4.6	1.2	52.9	24.7	11.9
2mm	56.6	34.0	4.1	0.9	52.7	23.8	11.0
BS	56.9	35.0	4.8	1.2	54.2	25.2	11.2
RobustA	57.3	32.1	2.1	0.6	53.5	22.1	10.4
RobustB	56.9	31.9	2.1	0.6	53.1	21.9	10.3

Table 5.10.: OAR values of the summed plans from BK007.

Summed Plan	CochleaL		CochleaR	
Nominal dose[Gy (RBE)]	$D_{2\%}$	Mean	$D_{2\%}$	Mean
RSL	31.4	21.1	35.1	17.7
2mm	26.7	17.5	33.2	15.8
BS	29.2	19.4	33.9	17.0
RobustA	26.4	16.7	33.5	15.6
RobustB	26.2	16.6	33.3	15.5

Table 5.11.: Additional OAR values of the summed plans from BK007.

Both left and right cochlea were analyzed as well. While the left cochlea overall had a higher average dose, the right cochlea showed a higher $D_{2\%}$. This is due to a small part of the right cochlea being directly located in the path of one of the beams, resulting in the higher maximum dose. As seen in table 5.11 the use of alternative margin concepts led to lower values for $D_{2\%}$ as well as the average dose and thus better sparing in both cochleae.

The cochlea serves as an example for how the reduction of the used margin directly resulted in a lower dose exposition to an organ which, while not directly located next to the tumor, still received a significant dose due to its proximity to the beam paths. This could also be observed on basis of the average dose to the 'External' ROI, which was highest for the RSL plan, followed in order by the beam-specific, 2mm, RobustA and lastly RobustB plans. Figure 5.12 illustrates the difference for the patient body when using a robust approach instead of a 5mm margin.

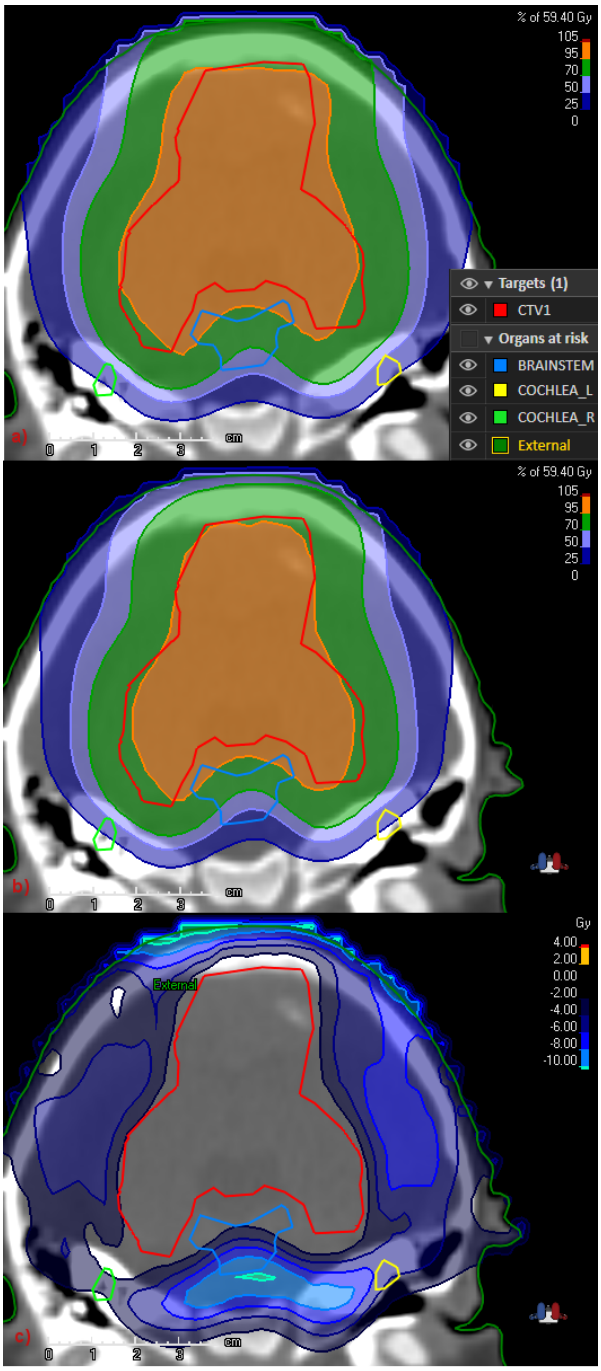

Figure 5.12.: Summed plan comparison for patient BK007. a) 5mm margin b) Robust optimization with additional OAR objectives c) Dose difference map.

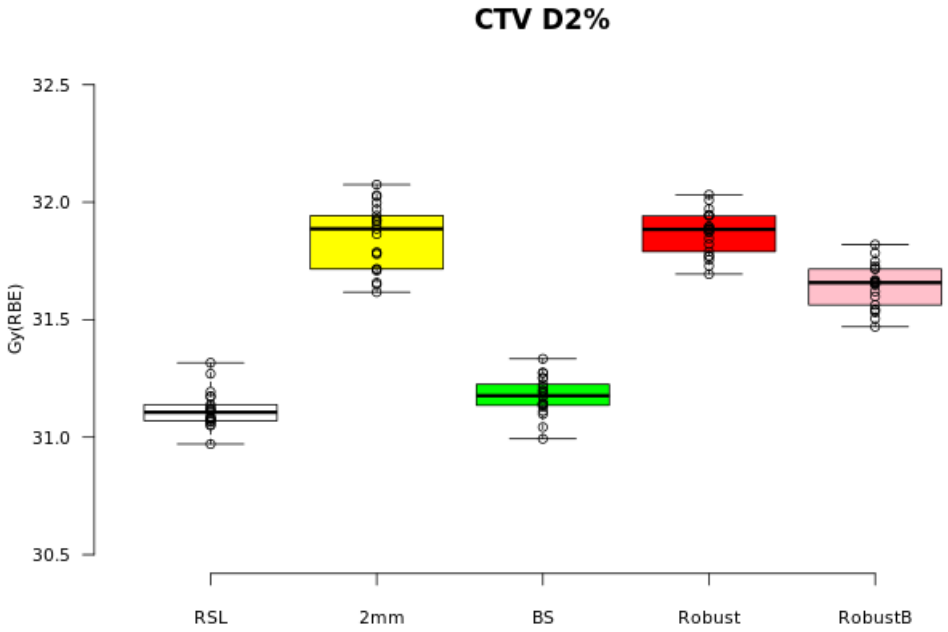

Figure 5.13.: Box and Whiskers plot of the $D_{2\%}$ of the CTV. (BK007, Series 1)

Robust Evaluation

Series 1

The results for Series 1 of the examined patient are listed in the appendix. The median dose $D_{50\%}$ of the CTV fulfilled the prescription dose of 30.6 Gy (RBE) within a range of less than 0.5% for all plans except the RobustA plan, which deviated from the RSL plan by up to 1%. As seen in figure 5.13, the $D_{2\%}$ was highest for the 2mm and RobustA plan at 31.9 Gy (RBE), followed by the RobustB plan. All margin concepts led to similar fluctuations of around ± 0.2 Gy (RBE), with the 2mm plan showing the highest deviations. The overall worst case perturbed scenarios all came from shifts in cranio-caudal direction. In the two robust plans, this shift combined with underestimating the density led to the highest perturbed values for $D_{2\%}$, while overestimating the density led to higher values in the other plans. For all plans and perturbation scenarios, the $D_{2\%}$ stayed below 105% of the prescription dose.

The behavior of $D_{98\%}$ and $V_{95\%}$ of the CTV under the influences of perturbations

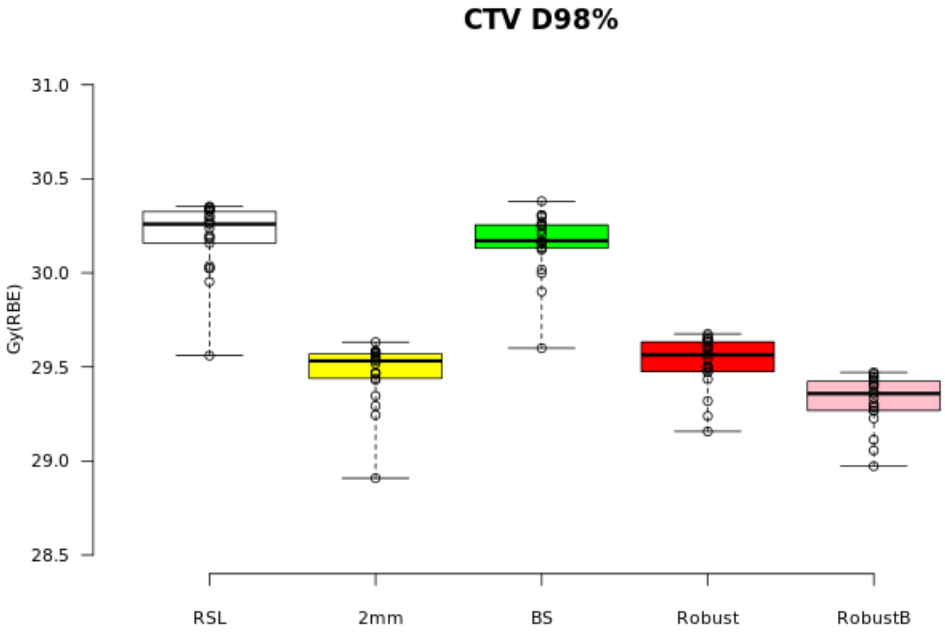

Figure 5.14.: Box and Whiskers plot of the $D_{98\%}$ of the CTV. (BK007, Series 1)

showed the target coverage that can be achieved. While the $V_{95\%}$ was above 99% for all nominal scenarios, it went to around or below 98% in the perturbation scenarios of the two robust approaches and the 2mm plan. As seen in 5.14, the $D_{98\%}$ showed less deviation from the nominal scenario for the two robust approaches, with the 2mm plan leading to the highest deviations. The lowest value of $D_{98\%}$ for all plans resulted from the same worst case scenario, a 0.2 cm shift in cranio-caudal direction while underestimating the density. This was the same worst case scenario as the one for the robust plans regarding the $D_{2\%}$.

The RSL plan led to the highest dose values for both the $D_{2\%}$ and the mean dose of the brainstem at 30.6 and 24.1 Gy (RBE), respectively. However, it also led to the lowest deviations from the nominal scenario. For the $D_{2\%}$, the dose value fluctuated 1.5% for the RSL plan, 3% for the 2mm and BS plans, and 4.5% for the two robust approaches. The mean dose behaved similarly, with the RSL plan leading to a range of 13% for the RSL plans, 16-17% for the 2mm and BS plans, and 26% for the robust approaches. Due to the high difference in the nominal scenarios, the worst case scenarios of the robust approaches at 21 Gy (RBE) still led to a lower dose than the lowest dose scenario of the RSL plan at 22 Gy (RBE). The additional robust objective to the brainstem in the RobustB plan was noticeable in the slightly lower dose values compared to the

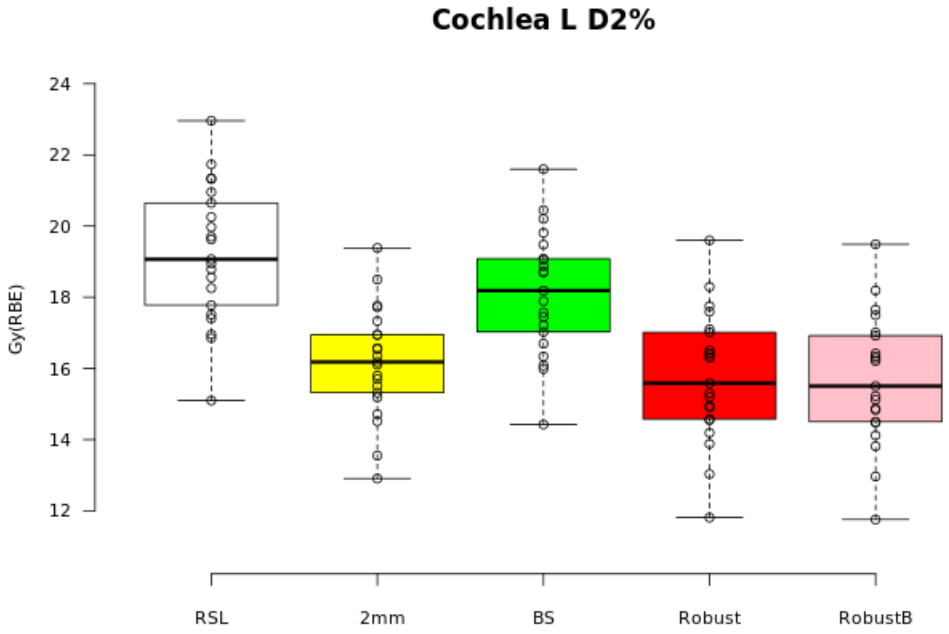

Figure 5.15.: Box and Whiskers plot of the $D_{2\%}$ of the left cochlea. (BK007, Series 1)

RobustA plan. Its worst case scenario results from a 0.2 cm shift in cranio-caudal while overestimating the density for all plans. For the $D_{2\%}$, the highest values were also caused by shifts in the cranio-caudal direction for all plans except the RSL plan.

The $D_{2\%}$ values of the cochleae are illustrated in figures 5.15 and 5.16. Especially for the left cochlea, the robust approaches led to significantly lower dose values, with their nominal value being lower by 3.5 Gy (RBE) and 1 Gy (RBE), respectively. Likewise, the average dose values are lower by 3 and 2 Gy (RBE).

For examining the chiasm, it again has to be noted that this OAR was located far away from the tumor and also not directly in a beam path, therefore receiving low doses. Both $D_{2\%}$ and mean dose were highest in the nominal case for the RSL plan, followed by the BS, 2mm, RobustA and RobustB plans. The nominal dose values of the $D_{2\%}$ and mean dose were significantly lower for the robust plans at 1.9 instead of 4.7 Gy (RBE). The fluctuations ranged between 80% and 110% of the nominal value for all margin concepts. Thus, the perturbed scenarios of the RobustA and RobustB scenarios led to values within a 2 Gy (RBE) range, while the RSL plan led to values within a 5 Gy (RBE) range. The ranges for the BS plan and

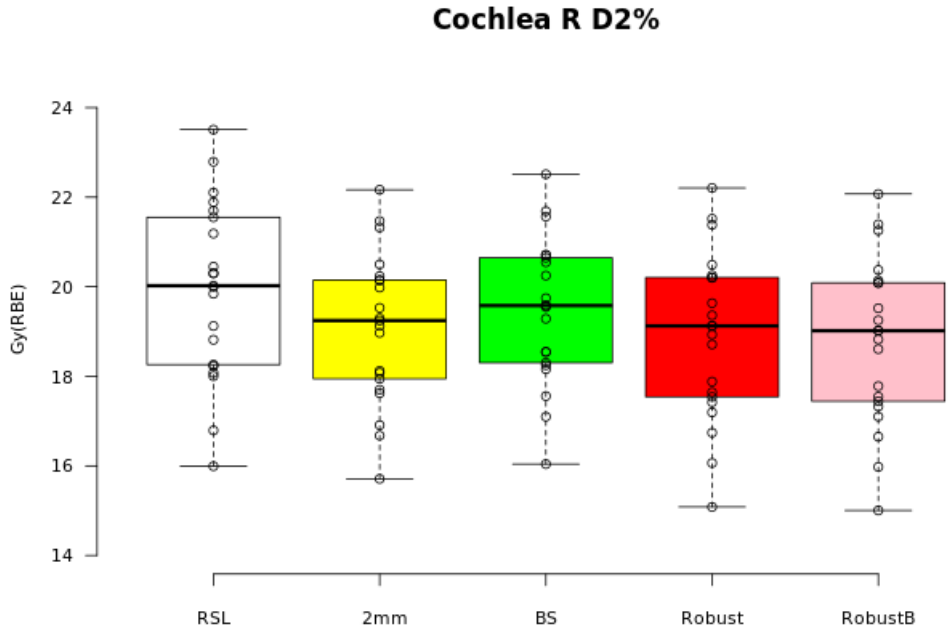

Figure 5.16.: Box and Whiskers plot of the $D_{2\%}$ of the right cochlea. (BK007, Series 1)

2mm plan were both around 3.7 Gy (RBE). In a similar fashion, the range of the mean dose was around 0.4 Gy (RBE) for the robust approaches and 1 Gy (RBE) for the other plans. Thus, it can be concluded that the robust approaches did lead to the most robust sparing of the chiasm. All plans had the same worst case scenario for both $D_{2\%}$ and mean dose, a 0.2 cm shift in cranio-caudal direction while overestimating the density.

The $D_{2\%}$ of the Spinal Cord in the nominal case was the highest for the RSL plan at 31.5 Gy (RBE), followed by the BS, 2mm, RobustA and RobustB plans, of which the latter led to 30 Gy (RBE). The former three plans led to fluctuations of around $\pm$0.3Gy (RBE). The robust plans which achieved the lower nominal dose saw the $D_{2\%}$ fluctuate within a range of around $\pm$1Gy (RBE). However, the worst case scenarios of the robust plans led to a dose similar to the minimal dose values of the other three plans. The results for the mean dose to the spinal cord were similar. The highest nominal dose came from the BS plan, followed by the RSL and 2mm plan. The two robust approaches led to a mean dose that was lower by around 3 Gy (RBE), so that their worst case scenarios were comparable to the lowest doses of the other plans at around 16 Gy (RBE). The overall behaviour of the dose to the spinal cord can be explained with the expansion of the PTV to

achieve symmetrical bone irradiation in Series 1, which was done for the RSL, BS and 2mm plans but not for the robust approaches. As such, the robust plans led to slightly higher deviations from the nominal dose under perturbations, but achieved lower dose values overall.

The average dose to the External ROI, which gives a rough indication of the general dose the patient is exposed to, was highest for the RSL plan at 7.4 Gy (RBE), followed by the BS, the 2mm, the RobustA and finally the RobustB plan at 6.3 Gy (RBE). This agrees with the used margin length and confirms that the robust approach succeeded in lowering the overall dose.

Overall, the robust approaches succeeded in sparing the OARs, leading to lower values of $D_{2\%}$ and a lower average dose for all OARs. The higher relative fluctuations compared to the other plans were acceptable, as the worst case scenarios of the robust approaches still led to a dose better than or comparable to the lowest possible doses of the other plans. The CTV coverage was minimally worse, although still acceptable, as shown by lower values of $D_{98\%}$ and $V_{95\%}$. This is partly a result of the additional PTV volume used to guarantee symmetrical bone irradiation, which was not used for the robust approaches, as those directly use the CTV. Also noticeable is the fact that, while the differences often were small, the additional robust objectives in the RobustB plan always led to lower dose values, both when it comes to CTV coverage and OAR sparing.

Series 2

The complete results for Series 2 of the examined patient are listed in the appendix. As was the case in Series 1, the $D_{50\%}$ of the CTV fulfilled the prescription dose, which is 19.8 Gy (RBE) for Series 2, within a range of 0.5% for all plans except the RobustA plan, which had a higher nominal dose at 19.9 Gy (RBE). The RobustA plan also technically led to the highest nominal value of $D_{2\%}$ at 20.5 Gy (RBE). For all plans, the scenario with the highest $D_{2\%}$ was one with a 0.2 cm shift in anterior-superior position. The dose value of $D_{2\%}$ stayed below 105% of the prescription dose even in the worst case scenario of all plans.

The $D_{98\%}$ of the CTV in the nominal and worst case scenario is listed in table 5.12. The robust approaches had slightly lower target coverage, and were affected differently by the perturbation scenarios. They were lowest for a -0.2 cm shift in anterior-superior and overestimation of the density, while a +0.2 cm shift and underestimation of the density led to the lowest values in the other plans. The

Series 2, CTV, $D_{98\%}$				
Margin	nominal[Gy (RBE)]	worst case[Gy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	19.5	19.4	z: 0.2; 3.5	z: 0.2; 0
2mm	19.5	19.1	z: 0.2; 3.5	z: 0.2; 0
BS	19.5	19.1	z: 0.2; 3.5	z: 0.2; 0
RobustA	19.3	18.8	z: -0.2; -3.5	z: -0.2; 0
RobustB	19.2	18.6	z: -0.2; -3.5	z: -0.2; 0

Table 5.12.: Worst case scenarios of the $D_{98\%}$ of the CTV.

Series 2, BS, $D_{2\%}$				
Margin	nominal[Gy (RBE)]	worst case[Gy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	19.7	19.9	y: 0.2; -3.5	x: 0.2; -3.5
2mm	19.6	19.8	y: 0.2; -3.5	x: 0.2; -3.5
BS	19.7	19.9	y: 0.2; -3.5	-x: 0.2; -3.5
RobustA	19.9	20	x: -0.2; -3.5	y: 0.2; -3.5
RobustB	19.7	19.9	x: -0.2; -3.5	y: 0.2; -3.5

Table 5.13.: Worst case scenarios of the $D_{2\%}$ of the brainstem.

$V_{95\%}$ behaved similarly to the $D_{98\%}$, as the robust plans fluctuated by around 2%, while the 2mm and BS plans fluctuated by around 1% and the RSL plan by 0.5%. Likewise, the same scenarios led to the highest deviations from the nominal value.

The $D_{2\%}$ of the brainstem are listed in table 5.13. As opposed to the $D_{98\%}$ of the CTV, the worst case scenarios were similar for all margin concepts. Together with the worst case scenarios of the $D_{2\%}$ (see appendix), it can be seen that the scenarios leading to the highest dose values are very similar regardless of the margin concept. However, the scenarios that impact the brainstem $D_{2\%}$ the most differ between the robust and the other approaches. The highest average brainstem dose resulted from the RSL plan and the lowest from the 2mm plan, although the relative difference of around 4%was small when compared to the differences of over 20% that could be seen in Series 1. Overall, the dose to the brainstem only changed very slightly depending on the plan used.

From Series 2 onwards, the chiasm values of $D_{2\%}$ and average dose were below 0.5 Gy (RBE), making meaningful comparison difficult. It is noted that the RSL plan led to the highest nominal values, while the RobustB plan succeeded in having the lowest nominal dose and the lowest absolute fluctuation range for both $D_{2\%}$ and the average dose.

Both cochleae profited from alternative margin concepts, with their respective

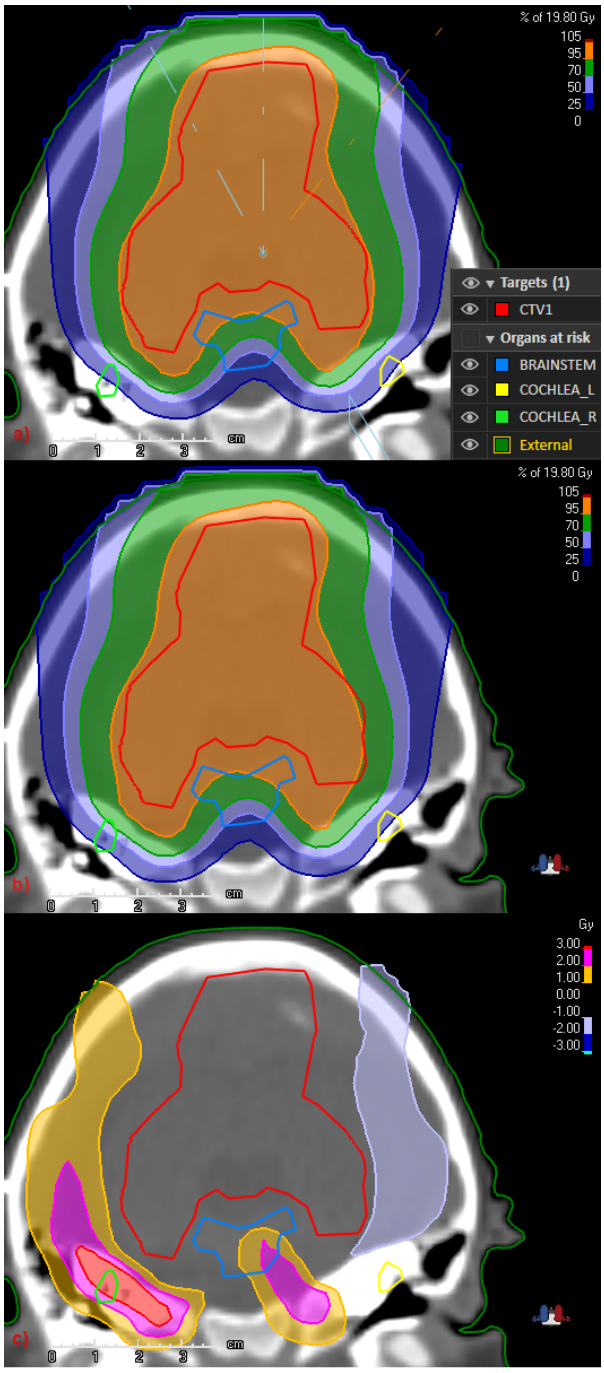

Figure 5.17.: Dose distribution for robust optimization in series 2 of patient BK007 a) in the nominal scenario b) in the (x = -0.2 cm, d = -3.5%) perturbed scenario. c) Dose difference map.

$D_{2\%}$ reduced by around 1 Gy (RBE) when using an alternative margin concept. The corresponding fluctuation ranges were ±4 Gy (RBE) and for both cochleae, all margin concepts shared the same worst case scenario. As they were located behind the tumor, the highest doses occured when overestimating the density while applying a shift along the left-right direction. The effects of the density overestimation and an isocenter shift in the right direction can be seen in figure 5.17, where the right cochlea received a significant amount of additional dose.

For the spinal cord, the $D_{2\%}$ was lowest for the 2mm plan at 18.7 Gy (RBE), although with a range of ±1.5 Gy (RBE). The robust plans led to the highest nominal $D_{2\%}$ at >19.5 Gy (RBE) with a similar range. The average spinal cord dose was the lowest for the 2mm plan at 6.6 Gy (RBE) as well. Without the additional PTV margin for symmetrical bone irradiation, the robust approaches did not outperform the other three plans anymore as it was the case in Series 1, instead leading to comparable results.

However, the average dose to the External was still lowest in RobustB and RobustA at 3.3 Gy (RBE), followed by the 2mm plan and the BS plan at 3.5 Gy (RBE), and the RSL plan at 3.7 Gy (RBE).

Series 3

The $D_{50\%}$ of the CTV fulfilled the prescription value within a range of 0.5% for all plans and scenarios. The $D_{2\%}$ was highest for the RobustA plan, which was also the case for Series 1 and 2, although the practical dose differences to the other plans were in the range of 0.01 Gy and as such all but meaningless in a practical sense. The fluctuations were around 1% for all plans. Likewise, the absolute differences between the individual perturbed scenarios were small, but the worst case scenarios was still the same for all plans except the BS plan, namely the 0.2 cm isocenter shift in anterior-posterior direction and 3.5% density perturbation which was also responsible for many worst case scenarios in Series 2. The $D_{98\%}$ could not be used in a meaningful way for this patient in Series 3, as the CTV reduction, in order to facilitate spinal cord sparing, was too large to evaluate the $D_{98\%}$.

When looking at the brainstem, it can be seen that the robust approaches led to a minimally lower $D_{2\%}$ and average dose, while the RSL plans had the highest values for both, as was the case in series 2.

The results for the chiasm differed from the results in the previous series insofar as

Series 3, Left Cochlea, $D_{2\%}$				
Margin	nominal[cGy (RBE)]	worst case[cGy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	165.8	230.9	x: 0.2; -3.5	z: -0.2; -3.5
2mm	151.2	213.9	x: 0.2; -3.5	z: -0.2; -3.5
BS	154.7	217.5	x: 0.2; -3.5	z: -0.2; -3.5
RobustA	137.1	205.5	x: 0.2; -3.5	z: -0.2; -3.5
RobustB	136.5	204.6	x: 0.2; -3.5	z: -0.2; -3.5

Table 5.14.: Worst case scenarios of the $D_{2\%}$ of the left cochlea, dose values in cGy (RBE).

the 2mm and BS plan achieved a similar dose reduction as the robust approaches when compared to the RSL plan, along with the reduction of the fluctuation range. However, this took place at a dose level of several cGy (RBE), making it not significant in any practical sense.

The left cochlea showed a behaviour that has been common amongst OARs not directly affected by the tumor in this study. As seen in table 5.14, the robust approaches led to the lowest nominal and perturbation values. The absolute fluctuation ranges were roughly equal for all margin concepts. The average dose behaved similarly, where the 2mm and BS plans achieved doses that are lower by 10% and the robust approaches lead to dose values that are 25% lower than the nominal RSL value of 1 Gy (RBE). Similar results were observed for the right cochlea, where the RSL plan also led to the highest nominal and perturbed values, while they were lowest for the robust approaches for both the $D_{2\%}$ and the mean dose, respectively.

The spinal cord values were highest for the BS plan and the two robust plans at 2.1 Gy (RBE), of which the latter was expected due to the innate treatment strategy of this series. The higher BS value came from the fact that for this specific patient, the PTV underwent modification to spare the spinal cord in addition to the cutoff at the first vertebrae. This additional modification was only undertaken for the 2mm and RSL plan as the robust approaches never used such TechPTVs, and a direct comparison between BS and robust plans was desired. Regardless of the margin concept used, the deviation range of the $D_{2\%}$ amounted to around 1 Gy (RBE) and that of the average dose to 0.2 Gy (RBE).

Series 4, GTV, $D_{98\%}$				
Margin	nominal[cGy (RBE)]	worst case[cGy (RBE)]	worst case scen.[cm; %]	2nd worst case scen.[cm; %]
RSL	521.2	467.6	z: 0.2; 3.5	z: 0.2; 0
2mm	512.5	463.3	z: 0.2; 3.5	z: 0.2; 0
BS	530.8	503.7	z: -0.2; -3.5	z: -0.2; 0
RobustA	530.9	508.4	z: 0.2; -3.5	z: 0.2; 0
RobustB	528.4	506.9	z: 0.2; -3.5	z: 0.2; 0

Table 5.15.: Worst case scenarios of the $D_{2\%}$ of the left cochlea, dose values in cGy (RBE).

Series 4

In Series 4, the CTV used was the post-tumor bed which is meant to receive additional radiation through the three fractions of this series. The $D_{50\%}$ of this CTV fulfilled the prescription dose of 5.4 Gy (RBE) within a margin of 1% for all plans and scenarios. Due to the additional target volume modifications that were applied to the 2mm and RSL plans of this patient specifically, the $D_{2\%}$ was highest for the BS plan, which led to a nominal value that was slightly than that of the RSL plan. The other margin concepts led to values that were lower by around 0.5 Gy (RBE). As shown in table 5.15, $D_{98\%}$ was at its highest value for the BS and the two robust plans, with an increase of 1-2% in comparison to the RSL plan. This shows that the additional target volume modification had an influence on the CTV dose values.

The $D_{2\%}$ of the brainstem, was highest at 3.9 Gy (RBE) for the robust approaches. A possible explanation is that the cutoff of the CTV below the first vertebrae is particularly relevant for the target volume and beam angles of this patient, leading to the robust approaches having increased dose values as the other plans did not use any margin at the cutoff area. The absolute fluctuation ranges did not differ much between the margin concepts and amounted up to 1.6-1.7 Gy (RBE).

At values mostly below the cGy threshold, the chiasm did not receive any significant dose regardless of margin concept. The same applied to the cochleae.

The results of the spinal cord were similar to that of Series 3 in that the BS and the robust plans led to significantly higher doses. Their $D_{2\%}$ was higher at 2.4 Gy (RBE) compared to the 2.0 Gy (RBE) of the RSL plan. The relative fluctuation ranges of the $D_{2\%}$ were 83% for the 2mm and RSL plans and around 75% for the other margin concepts, which resulted in ranges of 1.6 -1.8 Gy (RBE).

5.3. Discussion

BK001 and BK007 were two patients that representated the two groups of patients within the collective. BK001 belonged to the group where robust optimization led to a very similar or an at most 1 Gy (RBE) lower $D_{98\%}$ of the GTV in the summed plan. Other patients where this was the case were BK002 and BK011. On the other hand, BK007 is part of the group where the $D_{98\%}$ of the GTV reached a by up to 1.5 Gy (RBE) higher value when using robust optimization rather than the standard 5mm margin, together with BK003, BK004, BK006 and BK010. In those patients, robust optimization overall led to additional target coverage as it was not necessary to make PTV modifications meant to spare certain OARs. The results were deemed clinically suitable in either case. The differences of less than 1 Gy (RBE) for a prescription dose of 59.4 Gy (RBE) are acceptable, as the dose is still sufficient to elicit a very similar response from the tumor. Thus, the two patients are a good representation of the entire collective.

Furthermore, the eight evaluated patients differed in tumor location and used different beam angles, resulting in different OARs being more affected by in different patients. Patients BK001, BK002, BK003, BK010 and BK011 received moderate to high doses to the hippocampii, while patients BK006 and BK007 received high doses to the cochleae. For BK004, the middle and inner ears were the high risk organs.

For all patients, the results of the evaluation show that the $D_{2\%}$ of the CTV never exceeded 107% of the prescription dose in any nominal or perturbed scenario, regardless of the margin concept used. In fact, even its maximum often barely exceeded the prescription dose. When looking at the $D_{98\%}$, it can be seen that 95% of the prescription dose was always reached in the Series 1 plans, regardless of perturbations and margin concept, while it was never reached in Series 2. This is at least partly a byproduct of the treatment strategy, which added an additional margin to the PTV to ensure symmetrical bone irradiation in Series 1. The lower target coverage in Series 2 as well as Series 3 and 4 was an result of various measures, such as using TechPTVs and cutting off part of the spinal cord volume, which had to be taken to spare high risk organs.

Comparing the different margin concepts showed that the standard 5mm margin had overall the highest CTV coverage for all patients, followed by the beam-specific margin, the 2mm margin and then the robust approaches. However, the differences are overall small enough so that the CTV coverage was still sufficient even in the robust plans. Furthermore, the robust plans showed a higher $D_{98\%}$ for the GTV in

Series 4 for many patients, as its 5.4 Gy (RBE) was applied directly to the GTV regardless of the margin concept. As the GTV values did not differ much if at all in the other Series, this often translated to a higher GTV coverage in the summed plan.

In terms of OAR sparing, the overall picture is similar. The robust approaches, especially with additional OAR objectives, generally delivered the lowest mean dose to brainstem and chiasm and lowest $D_{2\%}$ to the chiasm, as well as lower doses to OARs such as the hippocampii and the cochleae. They were followed by the 2mm and beam-specific margins. The highest dose volume parameters belonged to the RSL plans. The $D_{2\%}$ of the brainstem did not change significantly for any margin concept in most patients due to its proximity to the target volume. For the spinal cord, the 2mm margin and the robust approaches led to the lowest dose, with the 2mm margin leading to a lower $D_{2\%}$ and the robust approaches to a lower mean dose. The overall dose to healthy tissue, measured by the average dose to the External ROI, was lowest for the robust optimization plans at 6.1 - 11.3 Gy (RBE), higher for the 2mm and beam-specific margins at 6.7 - 12.3 Gy (RBE) and highest for the RSL margin at 7.3 - 13.3 Gy (RBE).

Investigation of the perturbed scenarios showed that the use of different margin concepts did not largely influence the error scenarios leading to the most extreme dose values. In most cases, the same scenarios with shifts in cranio-caudal and anterior-superior directions together with an overestimation or underestimation of the density were responsible for the highest positive deviations from the nominal scenarios. For OARs such as the hippocampus and the chiasm, it was common for the exact same scenario to be responsible for the worst case regardless of series or margin concepts within a single patient. In individual series, specific setup errors often led to a low target coverage or high OAR doses, contributing as much as or more to the deviation than range errors. This was particularly pronounced in setups where an isocenter shift in a certain direction moved an OAR into the beam path. However, during a typical treatment with multiple fractions those setup errors would partly cancel each other out, while systematic range errors are more likely to impact the overall treatment quality. This is the same conclusion as was reached for instance by McGowan in 2015, who analyzed the robustness of Chardoma and Chodrosarcoma plans [71].

In McGowan's study, voxel-based error-bar dose distributions (ebDD) were used to evaluate the plan robustness and create a robustness database. This database could in turn be used to show the effects of range and setup errors on the treatment plan and serve as a baseline of what constitutes an adequately robust plan. An

VOI	Mean range (%)	Mean setup (%)	$V_{eb}3\%$ range (%)	$V_{eb}5\%$ range (%)	$V_{eb}5\%$ setup (%)	$V_{eb}10\%$ setup
Brainstem	1–2	6.5–9	2.5–17	5	63–85	15–37.5
Chiasm	1–1.5	8–15	<5	0	($V_{eb}15\%$) <50	($V_{eb}17\%$) <4
CTV	1.5–2.5	5–8	17.5–28	2.5–11.5	32.5–72.5	3–25.8

Figure 5.18.: Example for a robustness database taken from McGowan, 2015. $V_{eb}3$, $V_{eb}5$, and $V_{eb}10\%$ refer to the volume receiving an error of 3, 5 and 10%. [71]

example for such a database is shown in figure 5.18, which shows the increased impact of setup errors in those plans. Direct comparison to the results of this thesis is difficult due to the use of ebDDs and the separate treatment of setup and range errors, however the same general ideas regarding fractionation can be seen when examining the perturbation scenarios where only an isocenter shift or only the density perturbation occured. Taking the left hippocampus of Series 1 for patient BK001 as an example, the $D_{2\%}$ in the nominal scenario of the RobustB approach was 23.7 Gy (RBE). The worst case scenario, a shift of (z = 0.2 cm, d = -3.5%), led to a dose of 26.7 Gy (RBE), while by themselves, shifts of (z = 0.2 cm) and (d = -3.5%) led to doses of respectively 26.1 and 24.7 Gy (RBE). By itself, this would indicate that the setup error would have a higher impact on the plan robustness. In a standard clinical settings however, the setup errors would blur each other out and increase the relative influence of the range errors.

A method of incorporating fractionation in the evaluation of worst case scenarios is described in detail by Lowe et. al. (2016), who uses the distribution of dose errors in the initial perturbation scenarios to form a probability density function. When using multiple fractions, the probability density function of each voxel can be seen as a convolution with itself, leading to the function coverging towards a normal distribution as the number of fractions increases. Estimated upper and lower bounds for the error estimation were calculated this way. The results showed that with 5 fractions, the error band already showed a relevant reduction compared to the single fraction case while agreeing with the simulated treatment course used for validation. As such, Lowe places emphasis on taking the effects of fractionation in account to avoid the creation of overly conservative plans when optimizing for robustness [72].

The use of robust optimization did not necessarily lead to lower fluctuation ranges.

In Series 1, the robust approaches had the highest fluctuation ranges for $D_{2\%}$ and $D_{98\%}$ of the CTV. In Series 2, the robust plans still overall had a slightly higher range than the RSL plans, but a lower range than the 2mm and beam-specific margins. Only when comparing the chiasm results, the robust plan with an optimization objective to the chiasm led both to the lowest nominal values and the lowest fluctuation ranges as the robust optimization aimed to fulfill the given objective even in the perturbed scenarios. Thus, the worst case dose values for the robust plan were similar to the nominal values of the non-robust plans.

Overall, all alternative margin concepts succeeded in reducing the dose delivered to OARs and the remaining body in general. In comparison to the baseline laid out by the RSL plan, the average dose to the body could be reduced by more than 0.5 Gy (RBE) by choosing either the 2mm or BS plan and at least 1 Gy (RBE) by using a robust approach for all patients. In some patients, the reduction was even higher, reaching up to 2 Gy (RBE) for BK003 and BK004. While beam-specific margins performed the closest to the RSL plans, they gave up very little target coverage while not suffering from high fluctuation ranges. As such, they seem to be a safe way of reducing the dose to healthy tissue. 2mm margins led to lower OAR doses, but did not spare the OARs as much as the robust optimization plans did and suffered highly from perturbations. Robust optimization succeeded the most in sparing OARs, especially those that were specified as robust optimization objectives. In particular it showed the best results in sparing the chiasm, an organ further away from the beam paths. It did not guarantee a lower fluctuation range for the dose values of the other OARs. As it is always advantageous for the OAR dose to be lower, a higher fluctuation range caused by low dose outliers scenarios is no cause for worry. This is in contrast to the CTV, where the delivered dose has to be within a certain range. While the robust plans led to highest $D_{98\%}$ fluctuation in Series 1, where they lack the bone irradiation margin, they showed a similar or lower fluctuation range than the RSL plans in other series. As demonstrated by the Series 2 results, the robust plans significantly outperformed at least the 2mm margin plans in robustness. In exchange for OAR sparing, robust optimization with the used settings did give up a slight amount of target coverage in some patients. It is possible that choosing a slightly larger isocenter shift and density perturbation in the robust optimization settings could lead to equal target coverage while still sparing the organs more than the 5mm margin plans.

6. Summary and Outlook

The goal of this study was the comparison of different margins in proton therapy in regards to target coverage and organ sparing, in particular when subject to uncertainties in form of isocenter shifts and density perturbations. It was conducted at the Medical University of Vienna working as research unit at the non-clinical research part, PEG, of MedAustron in Wiener Neustadt, Austria, with the use of RayStation 4.8.102 as treatment planning system. CT data sets of 8 ependymoma patients that were treated at the PSI in Switzerland served as basis of the treatment plans. Those patients were treated with a prescription dose of 59.4 Gy(RBE), which was divided in 4 Series of 17, 11, 2 and 3 fractions, with a fraction dose of 1.8 Gy(RBE). This split had several purposes. It ensured the symmetrical irradiation of the bone structure to avoid their future asymmetrical growth by using an extended margin volume in Series 1. Series 3 cut off the target volume below the first vertebrae of the spinal cord to spare it, and Series 4 served as a boost to the tumor bed region.

In total, five different margin concepts were investigated on the basis of those ependymoma patients. Those were the standard 5mm margin, a reduced 2mm margin, beam-specific margins and robust optimization with robust objectives applied either to only the CTV or the CTV plus the brainstem and chiasm. The range of the uncertainty scenarios for both approaches was set at ±2mm isocenter shifts and ±3,5% density perturbation for both approaches.

Comparison of those margin concepts was carried out on basis of the nominal plan and 20 corresponding perturbed scenarios. The scenarios included were ±2mm isocenter shifts in the six coordinate directions combined with density shifts of 0% and ±3,5% in addition to the scenarios with ±3,5% density perturbation, but no isocenter shift. Dose parameters of $D_{2\%}$, $D_{50\%}$, $D_{98\%}$ and $V_{95\%}$ for target volumes as well as $D_{2\%}$ and mean dose for OARs were examined. The robust evaluation was carried out using the possibility of Python scripting which is implemented in RayStation. The creation of that script for both the purpose of this study and as basis of a possible future clinical implementation of robust evaluation was the secondary goal of this thesis.

The robust evaluation script was successfully created in RayStation 4.8.102 and confirmed to work with the recently released RayStation 5. Updates for future versions might be necessary. For the purpose of this study, the script was implemented in a way where it calculated the perturbed doses, summed plans and extracted the dose parameters for all plans of a patient in one use. This led to computation times of up to 48 hours for some patients. However, the time needed for a singular treatment plan generally amounted to several minutes at most. Thus, it is indicated that the implementation of this or a similar robust evaluation tool into clinical routine is feasible.

Evaluation results show that robust optimization methods are successful in lowering the dose to OARs without compromising target coverage. In particular, the use of select OARs as robust optimization targets has been proven to be effective, as it led to a consistently lower mean brainstem dose. Furthermore, the change from the PTV to the CTV as optimization target leads to an overall lower dose to the patient body. The body receives at least 1 Gy (RBE) less dose when using robust optimization as opposed to its conservative 5mm margin counterpart. As such, all OARs that are not in close proximity to the tumor greatly profit from not using the PTV margin.

While it would go beyond the scope of this thesis, the logical next step would be a voxel-based calculation of error-bar dose distributions (ebDD), as described by Albertini[73]. This method has amongst others been used by Casiraghi in 2013[74], Harding in 2014[75], and McGowan in 2015[71]. Albertini's method is also based on the dose distributions that are calculated for the perturbed scenarios. However, instead of looking at the worst case scenarios for each target/OAR, the evaluation is carried out voxel by voxel. For each voxel, the maximum and minimum dose are subtracted to form the error bar corresponding to that voxel. To note is that in her work, the setup errors resulting in isocenter shifts and the range errors are handled independently from each other, leading to a standard (setup) error-bar dose distribution and a corresponding range error-bar dose distribution. The setup error-bar dose distribution is described by the following equation.

$$\Delta D^i_{randomerror} = Max(D^i_{+x}, D^i_{-x}, ..., D^i_{-z}, D^i_{nom}) - Min(D^i_{+x}, D^i_{-x}, ..., D^i_{-z}, D^i_{nom}) \tag{6.1}$$

For a given point i (a voxel) in the dose grid, $\Delta D^i_{randomerror}$ is the corresponding value in the error distribution. D^i_{nom} is the nominal dose which results from the scenario without perturbations, while D^i_{+x}, D^i_{-x},..., D^i_{-z} are the recalculated doses

of the perturbed scenarios with an isocenter shift respective in the $+x, -x, ..., -z$ direction. Doing those calculation for every voxel results in a three-dimensional distribution of dose variation. Similar to the creation of dose volume histograms, it is possible to make an error-bar volume histograms (EVHs) for relevant regions of interest. Those EVHs serve as an useful tool to evaluate the treatment quality in respects to robustness, where lower error values indicate high robustness against the influence of perturbations [73].

The separately handled range error-bar distribution is calculated by the following equation.

$$\Delta D^i_{systematicerror} = Max(D^i_{+HU}, D^i_{-HU}, D^i_{nom}) - Min(D^i_{+HU}, D^i_{-HU}, D^i_{nom}) \quad (6.2)$$

$\Delta D^i_{systematicerror}$ is the value in the distribution of errors that resulted from inaccuracies of the nominal HU values in the patient's CT. D^i_{+HU} and D^i_{-HU} are respectively the doses resulting from underestimating and overestimating the tissue density [73].

Implementation of the voxel-based ebDD would necessitate the implementation of a method to retrieve the relevant maximum and minimum doses from the RayStation plans. This would, similar to the robust evaluation tool used in this thesis, be done by creating a Python script to export the mentioned doses. Those could then be used to calculate the ebDD and the EVHs. The advantage of that method is that it leads to a more detailed evaluation and is less likely to overestimate the errors. Furthermore, the ebDD can also be used for summed plans as opposed to only the individual series. As such, the voxel-based edDD is the most logical follow-up to this thesis in terms of evaluating the dosimetric impact of robust treatment planning.

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A. Appendix

Included are the detailed results of the perturbed scenarios in % for the $V_{95\%}$ and Gy (RBE) for the other dose parameters. The isocenter shifts and density perturbations of the individual perturbed scenarios are given in table A.1. Used OAR abbreviations are Br. for the brainstem, Ch. for the chiasm, SC for the spinal cord, L. Hip. and R. Hip for the left and the right hippocampus, L. Co. and R. Co. for the left and right cochlea as well as Ext. for the External.

Scenario	Isocenter shift[mm]			Density perturbation[%]
	x	y	z	d
1	0	0	0	0
2	0	0	0	3.5
3	0	0	0	-3.5
4	2	0	0	0
5	2	0	0	3.5
6	2	0	0	-3.5
7	-2	0	0	0
8	-2	0	0	3.5
9	-2	0	0	-3.5
10	0	2	0	0
11	0	2	0	3.5
12	0	2	0	-3.5
13	0	-2	0	0
14	0	-2	0	3.5
15	0	-2	0	-3.5
16	0	0	2	0
17	0	0	2	3.5
18	0	0	2	-3.5
19	0	0	-2	0
20	0	0	-2	3.5
21	0	0	-2	-3.5

Table A.1.: Isocenter shifts and density perturbations of the perturbed scenarios.

Patient BK001															
S.1 RSL	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.4	30.6	30.1	99.9	31.2	28.3	2.8	0.5	28.9	8.5	27.7	15.4	21.4	11.4	4.7
2	31.6	30.7	30.1	99.9	31.3	26.9	1.1	0.2	29.1	8.6	25.4	13.8	18.6	8.7	4.5
3	31.5	30.6	30	99.9	31.2	28.9	6.1	1.0	28.8	8.5	28.7	16.1	24.4	13.3	4.8
4	31.5	30.6	30.1	99.9	31.2	28.4	3.2	0.6	28.9	8.5	28.3	17.2	19.3	9.6	4.7
5	31.5	30.7	30.1	99.9	31.3	27	1.2	0.2	29.1	8.6	26.6	15.7	16.7	7.1	4.5
6	31.5	30.6	30.1	99.9	31.1	29	5.7	1.1	28.8	8.5	29.4	17.9	23.2	11.4	4.8
7	31.5	30.6	30	99.9	31.2	28.1	3.1	0.5	29	8.6	26.2	13.4	23.7	13.3	4.7
8	31.5	30.7	30.1	99.9	31.3	26.6	1.2	0.2	29.3	8.6	23.5	11.9	20.9	10.4	4.5
9	31.5	30.6	30	99.8	31.2	28.7	6.1	1.0	28.9	8.5	27.4	14.1	26.1	15.2	4.8
10	31.6	30.7	30.1	100	31.3	28.5	3.1	0.6	29.1	8.6	27.8	15.6	21.7	11.4	4.7
11	31.6	30.7	30.1	100	31.3	27.2	1.4	0.2	29.2	8.7	25.8	14.1	18.7	8.8	4.5
12	31.5	30.6	30.1	100	31.2	29.1	6.7	1.1	29	8.6	29.4	16.2	24.9	13.2	4.8
13	31.5	30.6	30	99.8	31.2	28	2.6	0.4	28.7	8.4	26.8	15.2	21.3	11.4	4.7
14	31.5	30.7	30.1	99.8	31.3	26.5	1.0	0.1	29	8.5	24.8	13.6	18.5	8.6	4.5
15	31.5	30.6	30	99.8	31.1	28.7	5.5	0.9	28.6	8.4	27.9	15.9	24.3	13.3	4.8
16	31.5	30.6	30	99.5	31.2	28.7	3.6	0.6	27.6	7.1	28.9	17.1	23.2	12.8	4.7
17	31.7	30.7	30	99.6	31.4	27.4	1.6	0.2	27.8	7.2	27.2	15.5	21	9.9	4.5
18	31.6	30.6	30	99.6	31.3	29.3	7.7	1.2	27.4	7.1	30	17.8	26.3	14.7	4.8
19	31.5	30.7	30.1	100	31.2	27.7	2.0	0.4	29.9	9.9	25.4	13.6	19.9	10	4.7
20	31.5	30.7	30.1	100	31.2	26.3	0.8	0.1	29.9	10	23.8	12.1	16.3	7.5	4.5
21	31.5	30.6	30.1	100	31.2	28.4	4.5	0.8	29.9	9.9	27.5	14.2	22.7	11.8	4.8
S.1 2mm	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.3	30.6	30.0	99.5	30.9	27.7	2.6	0.5	28.4	8.1	25.6	14.2	19.9	10.3	4.5
2	31.3	30.7	30.0	99.5	31.0	26.2	1.1	0.2	28.5	8.2	23.8	12.7	17.2	7.8	4.3
3	31.3	30.6	29.9	99.4	31.0	28.4	5.4	0.9	28.3	8.1	26.8	14.9	22.8	12.1	4.6
4	31.3	30.6	29.9	99.5	31.0	27.8	2.6	0.5	28.4	8.1	26.8	16.0	18.0	8.7	4.5
5	31.3	30.7	29.9	99.6	31.0	26.4	1.1	0.2	28.6	8.2	25.0	14.5	14.9	6.4	4.3
6	31.3	30.6	29.9	99.5	30.9	28.4	5.2	1.0	28.3	8.1	27.7	16.7	21.1	10.3	4.6
7	31.3	30.6	29.8	99.3	31.0	27.5	2.8	0.5	28.4	8.1	24.3	12.4	22.2	12.1	4.5
8	31.3	30.7	29.8	99.2	31.1	25.9	1.1	0.2	28.6	8.2	21.9	10.9	19.0	9.4	4.3
9	31.3	30.6	29.8	99.2	31.0	28.2	5.5	0.9	28.3	8.1	25.6	13.1	24.5	13.9	4.6
10	31.3	30.7	30.0	99.5	31.0	27.9	2.7	0.6	28.6	8.2	26.6	14.4	20.1	10.3	4.5
11	31.4	30.7	30.0	99.6	31.0	26.6	1.4	0.2	28.7	8.3	24.4	13.0	16.7	7.9	4.3
12	31.4	30.6	30.0	99.5	31.0	28.6	5.9	1.0	28.4	8.2	27.7	15.0	23.3	12.0	4.6
13	31.3	30.6	29.9	99.4	31.0	27.4	2.3	0.4	28.2	8.0	25.1	14.0	19.9	10.3	4.5
14	31.2	30.6	29.9	99.4	31.0	25.8	0.9	0.1	28.4	8.1	23.1	12.5	16.8	7.7	4.3
15	31.3	30.6	29.9	99.4	30.9	28.1	4.9	0.8	28.2	8.0	26.2	14.7	22.6	12.2	4.6
16	31.4	30.6	29.9	99.4	31.0	28.2	3.3	0.6	26.8	6.8	27.2	15.9	21.9	11.6	4.5
17	31.5	30.7	29.8	99.3	31.0	26.8	1.6	0.2	27.0	6.8	25.5	14.3	19.3	8.9	4.3
18	31.4	30.6	29.9	99.2	31.0	28.8	6.9	1.1	26.7	6.7	28.6	16.5	24.7	13.4	4.6
19	31.3	30.6	29.9	99.7	30.9	27.1	1.9	0.4	29.5	9.5	23.5	12.5	18.4	9.0	4.5
20	31.3	30.7	29.9	99.7	31.0	25.6	0.8	0.1	29.6	9.6	22.3	11.1	15.0	6.7	4.3
21	31.3	30.6	29.7	99.6	31.0	27.8	4.0	0.7	29.6	9.5	25.7	13.2	21.3	10.7	4.6

S.1 BS	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.2	30.6	30.0	99.5	31.0	27.9	2.6	0.5	28.9	8.5	27.7	15.4	21.4	11.4	4.7
2	31.3	30.7	30.0	99.5	31.1	26.4	1.1	0.2	29.1	8.6	25.4	13.8	18.6	8.7	4.5
3	31.2	30.6	29.9	99.4	31.0	28.5	5.6	0.9	28.8	8.5	28.7	16.1	24.4	13.3	4.8
4	31.3	30.6	29.9	99.5	31.0	28.0	3.0	0.5	28.9	8.5	28.3	17.2	19.3	9.6	4.7
5	31.2	30.7	30.0	99.6	31.0	26.6	1.1	0.2	29.1	8.6	26.6	15.7	16.7	7.1	4.5
6	31.3	30.6	29.8	99.4	31.0	28.6	5.4	1.0	28.8	8.5	29.4	17.9	23.2	11.4	4.8
7	31.3	30.6	29.8	99.2	31.1	27.7	2.9	0.5	29.0	8.6	26.2	13.4	23.7	13.3	4.7
8	31.3	30.7	29.9	99.2	31.1	26.2	1.2	0.2	29.3	8.6	23.5	11.9	20.9	10.4	4.5
9	31.3	30.6	29.7	99.2	31.0	28.3	5.7	0.9	28.9	8.5	27.4	14.1	26.1	15.2	4.8
10	31.3	30.7	30.0	99.5	31.1	28.1	2.8	0.6	29.1	8.6	27.8	15.6	21.7	11.4	4.7
11	31.3	30.7	30.1	99.6	31.1	26.8	1.4	0.2	29.2	8.7	25.8	14.1	18.7	8.8	4.5
12	31.3	30.6	29.9	99.5	31.0	28.7	6.2	1.1	29.0	8.6	29.4	16.2	24.9	13.2	4.8
13	31.2	30.6	29.9	99.4	31.0	27.6	2.4	0.4	28.7	8.4	26.8	15.2	21.3	11.4	4.7
14	31.2	30.7	30.0	99.5	31.0	26.1	0.9	0.1	29.0	8.5	24.8	13.6	18.5	8.6	4.5
15	31.2	30.6	29.8	99.4	31.0	28.3	5.1	0.8	28.6	8.4	27.9	15.9	24.3	13.3	4.8
16	31.4	30.6	29.9	99.4	31.0	28.4	3.5	0.6	27.6	7.1	28.9	17.1	23.2	12.8	4.7
17	31.4	30.7	29.9	99.5	31.1	27.0	1.6	0.2	27.8	7.2	27.2	15.5	21.0	9.9	4.5
18	31.4	30.6	29.9	99.4	31.0	29.0	7.1	1.2	27.4	7.1	30.0	17.8	26.3	14.7	4.8
19	31.2	30.6	29.8	99.7	31.0	27.3	1.9	0.4	29.9	9.9	25.4	13.6	19.9	10.0	4.7
20	31.3	30.7	29.9	99.7	31.1	25.8	0.8	0.1	29.9	10.0	23.8	12.1	16.3	7.5	4.5
21	31.3	30.6	29.6	99.5	31.0	27.9	4.1	0.7	29.9	9.9	27.5	14.2	22.7	11.8	4.8
S.1 RobA	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.0	30.6	29.7	99.5	30.9	27.8	2.6	0.5	28.6	8.1	26.4	14.1	20.3	10.2	4.2
2	31.1	30.6	29.7	99.5	31.0	26.4	1.1	0.2	28.8	8.2	24.1	12.6	17.0	7.7	4.1
3	31.1	30.5	29.6	99.3	30.9	28.4	5.6	0.9	28.7	8.1	27.3	14.7	23.7	12.0	4.3
4	31.1	30.6	29.5	99.2	30.9	27.9	3.1	0.5	28.9	8.2	27.2	15.8	18.8	8.6	4.2
5	31.1	30.6	29.6	99.3	31.0	26.5	1.1	0.2	28.9	8.2	25.1	14.4	14.9	6.3	4.1
6	31.1	30.5	29.4	98.9	30.9	28.5	5.5	1.1	28.8	8.1	28.1	16.5	22.5	10.3	4.3
7	31.1	30.6	29.5	99.0	31.0	27.5	2.9	0.5	28.5	8.1	24.4	12.2	22.2	12.0	4.2
8	31.1	30.6	29.5	99.1	31.1	26.1	1.2	0.2	28.7	8.1	21.9	10.8	19.1	9.3	4.1
9	31.1	30.5	29.4	98.9	31.0	28.2	5.7	0.9	28.5	8.0	25.9	12.9	25.2	13.8	4.3
10	31.1	30.6	29.7	99.6	31.0	28.0	2.8	0.6	28.9	8.2	26.5	14.2	20.8	10.3	4.2
11	31.2	30.6	29.8	99.6	31.0	26.7	1.3	0.2	29.1	8.3	23.9	12.8	17.1	7.8	4.1
12	31.1	30.6	29.6	99.4	30.9	28.6	5.9	1.1	29.0	8.2	27.9	14.8	24.2	12.0	4.3
13	31.1	30.6	29.6	99.3	31.0	27.5	2.4	0.4	28.4	8.0	25.6	13.9	20.2	10.2	4.2
14	31.1	30.6	29.6	99.2	30.9	26.0	0.9	0.1	28.6	8.1	23.1	12.3	16.9	7.6	4.1
15	31.0	30.5	29.5	99.1	30.9	28.1	5.2	0.8	28.4	8.0	26.3	14.6	23.2	12.1	4.3
16	31.2	30.6	29.6	99.1	31.0	28.3	3.4	0.6	27.0	6.8	27.6	15.7	22.1	11.5	4.2
17	31.2	30.6	29.6	99.1	31.0	26.9	1.6	0.2	27.4	6.8	25.5	14.1	19.3	8.8	4.1
18	31.1	30.6	29.5	99.1	30.9	28.9	7.2	1.2	27.1	6.7	28.6	16.3	25.8	13.3	4.3
19	31.1	30.6	29.6	99.4	30.9	27.1	1.9	0.4	29.8	9.6	24.0	12.4	18.6	9.0	4.2
20	31.2	30.6	29.7	99.5	31.0	25.7	0.8	0.1	29.8	9.6	21.8	11.0	14.8	6.6	4.1
21	31.1	30.5	29.4	99.2	31.0	27.8	4.2	0.7	29.9	9.5	25.9	13.0	22.1	10.6	4.3

S.1 RobB	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.1	30.6	29.7	99.5	31.1	26.8	1.0	0.2	28.7	8.1	23.7	13.0	18.9	9.5	4.1
2	31.2	30.6	29.7	99.4	31.2	25.1	0.5	0.1	28.9	8.2	22.0	11.5	15.4	7.0	4.0
3	31.1	30.5	29.6	99.2	31.2	27.7	1.7	0.4	28.8	8.1	24.7	13.7	20.6	11.2	4.2
4	31.1	30.6	29.5	99.2	31.2	26.9	1.3	0.3	28.9	8.2	25.5	14.7	16.9	7.9	4.1
5	31.2	30.6	29.5	99.2	31.2	25.3	0.6	0.1	29.0	8.2	23.3	13.2	13.4	5.7	4.0
6	31.1	30.5	29.4	99.0	31.1	27.8	2.2	0.5	28.8	8.2	25.5	15.4	19.8	9.6	4.2
7	31.1	30.6	29.5	99.0	31.2	26.6	1.1	0.2	28.5	8.1	21.6	11.3	20.8	11.0	4.1
8	31.2	30.6	29.4	98.9	31.2	24.9	0.6	0.1	28.8	8.2	20.2	9.8	17.4	8.5	4.0
9	31.0	30.5	29.3	98.9	31.1	27.4	1.8	0.4	28.6	8.1	23.6	12.0	22.0	12.8	4.2
10	31.2	30.6	29.7	99.5	31.2	27.1	1.2	0.3	28.9	8.3	24.0	13.2	18.9	9.4	4.1
11	31.3	30.6	29.8	99.5	31.3	25.5	0.7	0.1	29.1	8.3	23.0	11.7	15.2	7.1	4.0
12	31.1	30.6	29.6	99.4	31.2	27.9	1.9	0.5	29.1	8.2	25.4	13.9	21.0	11.1	4.2
13	31.1	30.6	29.6	99.2	31.1	26.4	0.9	0.2	28.5	8.0	24.0	12.9	18.7	9.5	4.1
14	31.2	30.6	29.6	99.1	31.1	24.7	0.5	0.1	28.7	8.1	20.9	11.3	15.4	7.0	4.0
15	31.0	30.5	29.5	99.1	31.1	27.3	1.6	0.4	28.5	8.0	24.3	13.6	20.3	11.3	4.2
16	31.2	30.6	29.6	99.1	31.2	27.4	1.3	0.3	27.1	6.8	26.1	14.6	20.6	10.8	4.1
17	31.3	30.6	29.5	99.0	31.3	25.8	0.8	0.1	27.4	6.8	23.7	13.0	17.9	8.2	4.0
18	31.2	30.6	29.5	99.1	31.2	28.2	2.2	0.5	27.2	6.7	26.7	15.4	22.5	12.6	4.2
19	31.1	30.6	29.6	99.3	31.1	26.2	0.7	0.2	29.8	9.6	21.1	11.4	16.7	8.2	4.1
20	31.2	30.6	29.6	99.2	31.2	24.4	0.4	0.1	29.8	9.6	20.4	9.9	13.1	6.0	4.0
21	31.1	30.5	29.4	99.2	31.1	27.1	1.4	0.3	29.9	9.5	22.6	12.0	18.5	9.7	4.2
S.2 RSL	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.5	19.9	19.1	98.7	20.2	18.2	1.5	0.4	12.6	4.2	14.7	6.6	12.1	5.9	2.8
2	20.5	19.9	19.1	98.6	20.2	17.3	0.7	0.2	12.8	4.0	12.7	5.9	10.3	4.5	2.7
3	20.5	19.9	19.2	98.8	20.2	18.6	3.4	0.7	13.1	4.6	16.4	7.1	14.2	7.0	2.9
4	20.6	19.9	19.4	98.8	20.2	18.3	1.8	0.4	13.6	4.4	15.7	7.8	10.3	4.8	2.8
5	20.6	19.9	19.4	98.8	20.2	17.4	0.6	0.2	13.3	4.1	14.5	7.1	8.7	3.6	2.7
6	20.5	19.9	19.4	98.9	20.1	18.7	3.3	0.8	13.9	4.7	17.0	8.4	13.1	5.9	2.9
7	20.6	19.9	18.8	97.9	20.3	18.0	1.8	0.4	12.8	4.2	12.9	5.4	13.6	7.0	2.8
8	20.6	19.9	18.8	97.9	20.2	17.1	0.8	0.2	12.7	4.0	11.0	4.8	11.5	5.5	2.7
9	20.5	19.8	18.8	98.1	20.3	18.5	3.5	0.7	13.6	4.5	14.7	5.9	15.0	8.2	2.9
10	20.6	19.9	19.3	98.9	20.2	18.4	1.9	0.5	13.3	4.4	14.9	6.8	11.9	5.9	2.8
11	20.6	19.9	19.2	98.7	20.2	17.5	0.8	0.2	13.1	4.1	12.5	6.1	10.0	4.6	2.7
12	20.5	19.9	19.3	99.0	20.3	18.7	3.8	0.8	14.0	4.7	16.7	7.3	14.0	6.9	2.9
13	20.5	19.9	19.0	98.4	20.2	18.0	1.5	0.4	12.6	4.1	14.1	6.4	12.2	5.9	2.8
14	20.5	19.9	19.0	98.4	20.2	17.1	0.6	0.2	12.9	3.9	13.0	5.7	10.3	4.4	2.7
15	20.5	19.8	19.1	98.4	20.2	18.4	3.2	0.7	12.8	4.5	15.4	7.0	13.7	7.1	2.9
16	20.6	19.9	18.7	97.9	20.2	18.4	2.1	0.5	11.0	3.4	16.4	7.6	13.5	6.7	2.8
17	20.6	19.9	18.7	97.8	20.3	17.6	1.0	0.2	11.1	3.2	14.3	6.8	11.7	5.2	2.7
18	20.6	19.9	18.7	97.8	20.2	18.8	4.3	0.9	11.2	3.7	17.4	8.2	15.2	7.9	2.9
19	20.5	19.9	19.3	99.3	20.2	17.9	1.2	0.3	14.9	5.2	12.7	5.7	10.7	5.1	2.8
20	20.5	19.9	19.2	99.2	20.2	16.9	0.4	0.1	14.9	4.9	11.2	5.1	8.8	3.8	2.7
21	20.5	19.9	19.3	99.3	20.3	18.3	2.5	0.6	15.7	5.6	14.7	6.1	12.8	6.1	2.9

S.2 2mm	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.3	19.9	18.8	98.1	20.2	17.6	1.3	0.4	11.7	3.6	13.3	5.9	11.1	5.3	2.6
2	20.3	19.9	18.7	97.7	20.2	16.6	0.6	0.2	11.5	3.4	11.7	5.3	9.2	4.1	2.5
3	20.3	19.8	18.8	98.0	20.2	18.1	2.9	0.6	12.3	3.9	14.6	6.5	13.0	6.4	2.6
4	20.4	19.9	19.0	98.4	20.2	17.7	1.4	0.4	12.7	3.7	14.3	7.1	9.5	4.4	2.6
5	20.4	19.9	18.9	98.2	20.2	16.7	0.5	0.2	12.0	3.5	13.3	6.3	7.8	3.3	2.5
6	20.3	19.8	19.0	98.5	20.2	18.2	2.8	0.7	13.2	4.1	15.6	7.6	12.0	5.3	2.6
7	20.3	19.8	18.3	96.7	20.2	17.4	1.4	0.4	11.7	3.6	11.6	4.9	12.6	6.4	2.5
8	20.4	19.9	18.2	96.0	20.2	16.4	0.6	0.2	11.7	3.3	10.1	4.3	10.6	5.0	2.5
9	20.3	19.8	18.4	96.6	20.3	17.9	2.9	0.6	12.6	3.9	13.2	5.4	13.9	7.5	2.6
10	20.4	19.9	19.0	98.4	20.2	17.8	1.5	0.4	12.5	3.7	13.7	6.1	11.0	5.3	2.6
11	20.4	19.9	18.8	97.9	20.3	16.8	0.6	0.2	12.0	3.5	11.6	5.5	9.0	4.1	2.5
12	20.4	19.8	19.0	98.3	20.2	18.2	3.2	0.7	13.4	4.1	15.0	6.6	13.0	6.3	2.6
13	20.3	19.8	18.6	97.5	20.2	17.4	1.2	0.3	11.7	3.5	12.6	5.8	11.2	5.4	2.5
14	20.3	19.9	18.5	97.1	20.2	16.4	0.5	0.2	11.4	3.3	11.9	5.1	9.2	4.0	2.5
15	20.3	19.8	18.6	97.4	20.2	17.9	2.7	0.6	12.0	3.8	14.0	6.4	12.7	6.4	2.6
16	20.4	19.9	18.2	97.0	20.2	17.9	1.8	0.5	9.9	2.9	14.7	6.8	12.4	6.1	2.6
17	20.4	19.9	18.1	96.7	20.2	17.0	0.9	0.2	9.7	2.7	13.3	6.1	10.7	4.7	2.5
18	20.4	19.8	18.2	97.2	20.2	18.3	3.7	0.8	10.3	3.1	16.0	7.4	14.1	7.2	2.6
19	20.3	19.9	19.0	98.4	20.2	17.2	1.0	0.3	14.3	4.5	11.5	5.1	9.8	4.6	2.6
20	20.4	19.9	18.8	98.1	20.3	16.2	0.3	0.1	13.8	4.2	10.0	4.5	7.9	3.5	2.5
21	20.3	19.8	18.9	98.3	20.2	17.7	2.1	0.5	15.2	5.0	13.2	5.6	11.8	5.6	2.6
S.2 BS	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.3	19.8	18.8	98.0	20.2	17.8	1.4	0.4	12.0	3.6	13.6	5.9	11.2	5.5	2.5
2	20.3	19.9	18.7	97.8	20.3	16.8	0.6	0.2	11.9	3.3	11.4	5.2	9.4	4.1	2.5
3	20.3	19.8	18.8	98.0	20.2	18.2	3.1	0.7	12.2	3.9	14.9	6.4	13.6	6.5	2.6
4	20.3	19.8	19.0	98.4	20.2	17.9	1.6	0.4	12.9	3.7	14.6	7.0	9.7	4.5	2.5
5	20.4	19.9	19.0	98.4	20.3	17.0	0.6	0.2	12.3	3.5	13.0	6.3	8.0	3.3	2.5
6	20.3	19.8	18.9	98.4	20.2	18.3	3.0	0.8	13.2	4.0	15.5	7.5	12.7	5.5	2.6
7	20.3	19.8	18.4	96.6	20.3	17.6	1.6	0.4	12.0	3.5	11.7	4.8	12.6	6.5	2.5
8	20.4	19.9	18.3	96.4	20.2	16.6	0.7	0.2	11.9	3.3	9.8	4.3	10.7	5.1	2.5
9	20.3	19.8	18.3	96.2	20.3	18.1	3.1	0.7	12.7	3.8	13.4	5.3	14.6	7.6	2.6
10	20.3	19.9	19.0	98.4	20.3	18.0	1.6	0.4	12.6	3.7	13.5	6.0	11.2	5.5	2.5
11	20.4	19.9	18.8	98.1	20.3	17.1	0.7	0.2	12.3	3.5	11.3	5.4	9.2	4.2	2.5
12	20.3	19.8	18.9	98.2	20.2	18.4	3.4	0.8	13.4	4.0	15.3	6.5	14.0	6.4	2.6
13	20.3	19.8	18.6	97.6	20.3	17.6	1.3	0.4	11.9	3.5	12.9	5.8	11.3	5.5	2.5
14	20.3	19.9	18.6	97.4	20.3	16.6	0.6	0.2	11.9	3.3	11.6	5.1	9.4	4.1	2.5
15	20.3	19.8	18.6	97.4	20.2	18.1	2.9	0.6	12.1	3.8	14.2	6.3	13.2	6.6	2.6
16	20.4	19.9	18.4	97.1	20.3	18.1	1.9	0.5	10.1	2.8	15.0	6.7	12.5	6.3	2.5
17	20.4	19.9	18.3	97.2	20.3	17.2	1.0	0.2	10.0	2.7	13.0	6.0	10.8	4.8	2.5
18	20.4	19.8	18.4	97.1	20.2	18.5	3.9	0.9	10.3	3.1	16.0	7.3	14.7	7.4	2.6
19	20.3	19.8	18.9	98.3	20.2	17.4	1.1	0.3	14.6	4.5	11.6	5.1	10.0	4.7	2.5
20	20.4	19.9	18.9	98.2	20.3	16.5	0.4	0.1	14.2	4.2	9.8	4.5	8.0	3.5	2.5
21	20.3	19.8	18.8	98.0	20.2	17.9	2.3	0.5	15.2	4.9	13.4	5.5	11.8	5.7	2.6

S.2 RobA	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.2	19.8	18.5	96.8	20.2	17.6	1.3	0.4	11.4	3.5	13.1	5.6	10.7	5.2	2.4
2	20.3	19.8	18.5	97.1	20.3	16.6	0.6	0.2	11.3	3.3	10.9	5.0	9.1	3.9	2.4
3	20.2	19.7	18.4	96.2	20.2	18.0	2.9	0.7	12.0	3.9	14.6	6.1	13.5	6.2	2.5
4	20.3	19.8	18.5	96.7	20.2	17.7	1.6	0.4	12.4	3.6	14.4	6.7	9.6	4.3	2.4
5	20.3	19.8	18.5	97.0	20.2	16.8	0.5	0.2	11.8	3.4	12.2	6.0	7.8	3.2	2.4
6	20.2	19.7	18.4	95.9	20.1	18.1	2.9	0.8	12.8	4.0	15.5	7.2	12.7	5.2	2.5
7	20.3	19.8	18.1	95.0	20.2	17.4	1.4	0.4	11.3	3.5	11.5	4.6	12.0	6.2	2.4
8	20.3	19.8	18.0	95.0	20.2	16.5	0.6	0.2	11.3	3.2	9.3	4.1	10.3	4.8	2.4
9	20.2	19.7	18.0	94.3	20.2	17.8	3.0	0.7	12.4	3.8	13.2	5.0	14.5	7.3	2.5
10	20.3	19.8	18.6	97.1	20.2	17.7	1.5	0.4	12.1	3.6	13.2	5.7	11.0	5.2	2.4
11	20.3	19.8	18.6	97.2	20.3	16.9	0.6	0.2	11.6	3.4	10.8	5.2	9.0	4.0	2.4
12	20.2	19.7	18.5	96.2	20.2	18.1	3.2	0.8	13.1	4.0	15.0	6.2	13.9	6.2	2.5
13	20.2	19.8	18.4	96.3	20.2	17.4	1.3	0.4	11.4	3.4	12.8	5.5	10.6	5.3	2.4
14	20.3	19.8	18.2	96.6	20.2	16.4	0.5	0.2	11.3	3.2	11.0	4.8	9.1	3.9	2.4
15	20.2	19.7	18.3	95.6	20.2	17.8	2.8	0.6	11.7	3.8	13.9	6.0	13.3	6.3	2.5
16	20.3	19.8	18.1	96.2	20.3	17.9	1.8	0.5	9.7	2.8	14.8	6.5	11.8	6.0	2.4
17	20.3	19.8	18.0	96.4	20.3	17.0	0.9	0.2	9.6	2.6	12.4	5.8	10.5	4.6	2.4
18	20.3	19.8	18.1	95.8	20.2	18.3	3.7	0.9	10.0	3.0	15.7	7.0	14.7	7.0	2.5
19	20.2	19.7	18.5	95.8	20.2	17.2	0.9	0.3	14.1	4.5	11.2	4.8	9.6	4.5	2.4
20	20.3	19.8	18.5	96.6	20.3	16.2	0.4	0.1	13.6	4.1	9.3	4.3	7.7	3.4	2.4
21	20.2	19.7	18.3	94.8	20.2	17.6	2.2	0.5	14.7	4.9	13.0	5.2	12.3	5.4	2.5
S.2 RobB	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.2	19.8	18.6	97.2	20.2	17.0	0.6	0.2	11.3	3.5	12.2	5.4	9.7	4.8	2.4
2	20.3	19.8	18.4	97.2	20.3	15.9	0.2	0.1	11.3	3.2	10.8	4.7	8.4	3.6	2.3
3	20.2	19.7	18.5	96.7	20.2	17.5	1.0	0.4	11.9	3.8	13.6	5.9	11.6	5.7	2.5
4	20.3	19.8	18.5	97.0	20.3	17.1	0.7	0.3	12.3	3.6	13.3	6.4	8.9	4.0	2.4
5	20.3	19.8	18.5	97.1	20.3	16.0	0.3	0.1	11.7	3.3	12.4	5.7	7.3	2.9	2.3
6	20.2	19.7	18.4	96.3	20.2	17.6	1.2	0.4	12.7	3.9	14.4	7.0	11.2	4.8	2.5
7	20.2	19.8	18.1	95.2	20.2	16.8	0.5	0.2	11.3	3.4	10.7	4.4	10.9	5.7	2.4
8	20.3	19.8	18.0	95.2	20.3	15.7	0.2	0.1	11.3	3.2	9.3	3.8	9.5	4.4	2.3
9	20.2	19.7	18.1	94.7	20.2	17.4	1.0	0.4	12.3	3.8	12.3	4.9	12.5	6.7	2.5
10	20.3	19.8	18.7	97.2	20.3	17.2	0.6	0.2	12.1	3.6	12.7	5.5	9.8	4.8	2.4
11	20.3	19.8	18.6	97.5	20.3	16.1	0.3	0.1	11.6	3.4	10.7	4.9	8.3	3.6	2.3
12	20.2	19.7	18.6	96.7	20.2	17.7	1.1	0.4	13.1	3.9	14.1	6.0	12.3	5.7	2.5
13	20.2	19.7	18.4	96.6	20.2	16.8	0.6	0.2	11.3	3.4	11.4	5.3	9.7	4.8	2.4
14	20.3	19.8	18.2	96.6	20.2	15.6	0.2	0.1	11.2	3.1	11.0	4.6	8.4	3.6	2.3
15	20.2	19.7	18.4	95.9	20.2	17.3	0.9	0.4	11.7	3.7	12.9	5.8	11.5	5.8	2.5
16	20.3	19.8	18.1	96.6	20.3	17.4	0.7	0.3	9.6	2.7	13.8	6.2	10.8	5.5	2.4
17	20.4	19.8	18.1	96.5	20.4	16.3	0.3	0.2	9.5	2.6	12.3	5.5	9.8	4.2	2.3
18	20.3	19.8	18.1	96.3	20.2	17.9	1.2	0.5	10.0	3.0	15.1	6.8	13.0	6.6	2.5
19	20.2	19.7	18.5	96.3	20.2	16.6	0.4	0.2	14.1	4.4	10.5	4.6	8.4	4.1	2.4
20	20.3	19.8	18.5	96.5	20.3	15.5	0.2	0.1	13.5	4.1	9.2	4.0	7.1	3.0	2.3
21	20.2	19.7	18.4	95.5	20.2	17.1	0.7	0.3	14.7	4.8	11.9	5.0	10.1	4.9	2.5

S.3 RSL	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.71	3.61	2.26	95.2	3.70	3.31	0.28	0.08	0.77	0.14	2.66	1.21	2.16	1.06	0.44
2	3.72	3.62	2.25	95.2	3.70	3.14	0.13	0.04	0.78	0.14	2.27	1.08	1.73	0.81	0.43
3	3.72	3.61	2.28	95.2	3.70	3.38	0.57	0.14	0.77	0.14	2.93	1.31	2.44	1.26	0.45
4	3.72	3.61	2.32	95.3	3.71	3.32	0.34	0.09	0.78	0.14	2.85	1.43	1.86	0.88	0.44
5	3.73	3.62	2.30	95.3	3.70	3.16	0.12	0.04	0.78	0.14	2.59	1.29	1.52	0.65	0.43
6	3.72	3.61	2.34	95.3	3.70	3.39	0.61	0.15	0.77	0.14	3.08	1.53	2.34	1.06	0.45
7	3.72	3.61	2.18	94.6	3.70	3.28	0.32	0.08	0.77	0.14	2.37	1.00	2.40	1.26	0.44
8	3.72	3.61	2.16	94.7	3.70	3.11	0.14	0.03	0.78	0.14	2.00	0.88	1.97	0.99	0.43
9	3.72	3.60	2.19	94.8	3.70	3.35	0.61	0.13	0.76	0.14	2.64	1.09	2.66	1.47	0.45
10	3.72	3.61	2.32	95.3	3.71	3.34	0.33	0.09	0.79	0.15	2.70	1.24	2.17	1.07	0.44
11	3.73	3.62	2.27	95.2	3.71	3.18	0.15	0.04	0.80	0.15	2.29	1.12	1.77	0.82	0.43
12	3.72	3.61	2.33	95.3	3.70	3.40	0.64	0.15	0.79	0.15	3.02	1.33	2.56	1.25	0.45
13	3.72	3.61	2.20	95.0	3.70	3.27	0.25	0.07	0.76	0.14	2.56	1.18	2.14	1.07	0.44
14	3.73	3.61	2.17	95.1	3.70	3.10	0.11	0.04	0.76	0.14	2.34	1.04	1.70	0.80	0.43
15	3.72	3.60	2.20	95.0	3.70	3.35	0.52	0.13	0.75	0.14	2.79	1.28	2.45	1.27	0.45
16	3.73	3.61	1.82	93.2	3.70	3.35	0.39	0.10	0.56	0.10	2.96	1.39	2.34	1.22	0.44
17	3.74	3.62	1.79	93.1	3.70	3.19	0.19	0.05	0.56	0.10	2.59	1.24	1.99	0.94	0.43
18	3.73	3.61	1.82	93.2	3.70	3.41	0.73	0.17	0.57	0.10	3.11	1.50	2.72	1.43	0.45
19	3.72	3.61	2.71	95.7	3.70	3.26	0.20	0.06	1.04	0.19	2.31	1.03	1.95	0.92	0.44
20	3.72	3.61	2.68	95.8	3.71	3.08	0.08	0.03	1.04	0.19	1.99	0.92	1.49	0.69	0.43
21	3.72	3.61	2.70	95.5	3.70	3.33	0.44	0.11	1.03	0.19	2.64	1.12	2.18	1.10	0.45
S.3 2mm	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.68	3.60	2.20	94.9	3.67	3.25	0.25	0.07	0.79	0.14	2.42	1.09	2.01	0.99	0.42
2	3.68	3.61	2.18	94.7	3.68	3.07	0.11	0.03	0.78	0.14	2.15	0.97	1.61	0.75	0.40
3	3.68	3.60	2.23	94.7	3.67	3.32	0.51	0.12	0.79	0.14	2.64	1.19	2.33	1.17	0.43
4	3.69	3.60	2.27	95.1	3.67	3.26	0.29	0.08	0.79	0.14	2.61	1.30	1.81	0.82	0.42
5	3.69	3.61	2.24	94.9	3.67	3.09	0.10	0.04	0.79	0.14	2.44	1.17	1.38	0.60	0.40
6	3.68	3.60	2.31	95.1	3.67	3.34	0.53	0.14	0.79	0.14	2.84	1.40	2.17	0.98	0.43
7	3.68	3.60	2.10	93.7	3.68	3.21	0.28	0.07	0.78	0.14	2.13	0.90	2.28	1.18	0.42
8	3.68	3.61	2.08	93.4	3.67	3.04	0.12	0.03	0.79	0.14	1.87	0.79	1.85	0.92	0.40
9	3.68	3.60	2.13	93.5	3.67	3.30	0.54	0.12	0.77	0.14	2.37	0.99	2.50	1.37	0.43
10	3.69	3.61	2.27	95.0	3.68	3.28	0.30	0.08	0.81	0.15	2.51	1.12	2.07	0.99	0.42
11	3.69	3.61	2.21	94.8	3.68	3.11	0.13	0.04	0.80	0.15	2.13	1.01	1.65	0.76	0.40
12	3.68	3.60	2.29	95.0	3.68	3.35	0.57	0.14	0.81	0.15	2.73	1.21	2.27	1.16	0.43
13	3.68	3.60	2.13	94.3	3.67	3.21	0.22	0.07	0.77	0.14	2.30	1.07	2.04	0.99	0.42
14	3.68	3.61	2.10	94.2	3.67	3.03	0.10	0.03	0.77	0.14	2.18	0.94	1.60	0.74	0.40
15	3.67	3.60	2.14	94.2	3.67	3.29	0.47	0.11	0.77	0.14	2.54	1.17	2.28	1.18	0.43
16	3.69	3.61	1.76	92.7	3.68	3.29	0.35	0.09	0.56	0.10	2.66	1.26	2.23	1.13	0.42
17	3.69	3.61	1.74	92.4	3.68	3.12	0.16	0.04	0.57	0.10	2.44	1.12	1.85	0.87	0.40
18	3.69	3.60	1.78	92.7	3.68	3.36	0.69	0.16	0.58	0.10	2.92	1.36	2.54	1.32	0.43
19	3.68	3.60	2.64	95.4	3.67	3.19	0.18	0.06	1.06	0.19	2.09	0.94	1.84	0.86	0.42
20	3.69	3.61	2.61	95.1	3.68	3.01	0.07	0.03	1.05	0.19	1.82	0.83	1.39	0.64	0.40
21	3.68	3.60	2.66	95.0	3.67	3.27	0.39	0.10	1.06	0.20	2.38	1.02	2.03	1.03	0.43

S.3 BS	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.68	3.60	2.23	94.8	3.67	3.27	0.26	0.08	0.79	0.15	2.43	1.08	2.08	1.01	0.42
2	3.68	3.61	2.19	94.7	3.68	3.11	0.12	0.04	0.80	0.15	2.10	0.97	1.65	0.75	0.40
3	3.68	3.60	2.23	94.5	3.68	3.34	0.54	0.13	0.79	0.15	2.73	1.17	2.33	1.19	0.43
4	3.68	3.60	2.30	95.0	3.68	3.28	0.31	0.09	0.80	0.15	2.67	1.29	1.80	0.83	0.42
5	3.69	3.61	2.27	95.0	3.68	3.12	0.11	0.04	0.80	0.15	2.35	1.17	1.47	0.61	0.40
6	3.68	3.60	2.31	95.0	3.67	3.35	0.57	0.15	0.79	0.15	2.89	1.38	2.35	1.01	0.43
7	3.68	3.60	2.12	93.5	3.68	3.24	0.29	0.07	0.79	0.15	2.16	0.90	2.25	1.19	0.41
8	3.69	3.61	2.12	93.5	3.69	3.07	0.13	0.03	0.80	0.15	1.78	0.79	1.86	0.92	0.40
9	3.68	3.60	2.14	93.3	3.68	3.32	0.56	0.12	0.79	0.14	2.44	0.98	2.57	1.39	0.43
10	3.68	3.61	2.30	94.9	3.68	3.30	0.30	0.08	0.81	0.15	2.46	1.11	2.09	1.00	0.42
11	3.69	3.61	2.25	94.8	3.69	3.14	0.13	0.04	0.81	0.15	2.06	1.01	1.71	0.77	0.40
12	3.68	3.60	2.30	94.8	3.68	3.37	0.60	0.15	0.81	0.15	2.82	1.19	2.57	1.18	0.43
13	3.68	3.60	2.16	94.3	3.68	3.24	0.23	0.07	0.78	0.14	2.36	1.06	2.00	1.01	0.41
14	3.68	3.61	2.13	94.4	3.68	3.06	0.10	0.03	0.78	0.14	2.10	0.94	1.63	0.75	0.40
15	3.67	3.60	2.16	94.0	3.68	3.31	0.49	0.12	0.77	0.14	2.58	1.15	2.31	1.20	0.43
16	3.69	3.61	1.79	92.7	3.68	3.31	0.37	0.10	0.58	0.11	2.74	1.25	2.22	1.15	0.42
17	3.69	3.61	1.76	92.6	3.68	3.15	0.17	0.05	0.57	0.11	2.35	1.12	1.91	0.87	0.40
18	3.68	3.60	1.79	92.7	3.68	3.38	0.69	0.16	0.59	0.11	2.90	1.35	2.64	1.35	0.43
19	3.68	3.60	2.67	95.1	3.68	3.22	0.19	0.06	1.06	0.20	2.08	0.93	1.88	0.87	0.42
20	3.69	3.61	2.65	95.2	3.69	3.05	0.08	0.03	1.05	0.20	1.78	0.83	1.43	0.65	0.40
21	3.68	3.59	2.66	94.7	3.68	3.29	0.42	0.10	1.06	0.20	2.49	1.00	2.11	1.04	0.43
S.3 RobA	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.67	3.60	2.28	94.2	3.67	3.27	0.25	0.08	0.82	0.15	2.40	1.06	2.09	0.97	0.41
2	3.68	3.60	2.25	94.5	3.69	3.10	0.12	0.04	0.83	0.15	2.08	0.95	1.66	0.72	0.39
3	3.66	3.59	2.30	93.8	3.67	3.33	0.55	0.13	0.82	0.15	2.71	1.15	2.48	1.15	0.42
4	3.67	3.59	2.34	94.0	3.67	3.28	0.32	0.09	0.82	0.15	2.65	1.26	1.79	0.80	0.41
5	3.67	3.60	2.32	94.1	3.68	3.12	0.11	0.04	0.82	0.15	2.33	1.15	1.42	0.59	0.39
6	3.66	3.59	2.34	93.3	3.66	3.34	0.59	0.15	0.82	0.15	2.86	1.35	2.26	0.97	0.42
7	3.67	3.60	2.16	93.0	3.68	3.24	0.29	0.07	0.82	0.15	2.14	0.88	2.21	1.15	0.41
8	3.68	3.60	2.17	93.2	3.69	3.07	0.12	0.03	0.82	0.15	1.76	0.77	1.85	0.89	0.39
9	3.67	3.59	2.19	92.6	3.67	3.31	0.57	0.13	0.82	0.15	2.44	0.96	2.58	1.34	0.42
10	3.68	3.60	2.35	94.5	3.69	3.30	0.30	0.09	0.84	0.15	2.44	1.09	2.09	0.97	0.41
11	3.68	3.60	2.30	94.5	3.69	3.14	0.13	0.04	0.85	0.16	2.05	0.99	1.67	0.74	0.39
12	3.67	3.59	2.37	93.9	3.67	3.36	0.61	0.15	0.84	0.15	2.80	1.17	2.55	1.14	0.42
13	3.66	3.59	2.21	94.0	3.68	3.23	0.23	0.07	0.80	0.14	2.34	1.04	1.97	0.97	0.41
14	3.67	3.60	2.18	94.2	3.68	3.06	0.10	0.04	0.81	0.14	2.08	0.92	1.62	0.72	0.39
15	3.66	3.59	2.22	93.2	3.67	3.30	0.50	0.12	0.80	0.14	2.55	1.13	2.41	1.16	0.42
16	3.68	3.60	1.82	92.4	3.68	3.31	0.37	0.10	0.60	0.11	2.71	1.22	2.20	1.10	0.41
17	3.68	3.60	1.80	92.6	3.69	3.15	0.17	0.05	0.60	0.11	2.33	1.09	1.85	0.84	0.39
18	3.67	3.59	1.85	92.1	3.67	3.37	0.69	0.17	0.60	0.11	2.86	1.32	2.67	1.30	0.42
19	3.67	3.59	2.72	94.5	3.67	3.21	0.19	0.06	1.10	0.20	2.05	0.91	1.88	0.84	0.41
20	3.68	3.60	2.69	94.9	3.69	3.04	0.08	0.03	1.10	0.20	1.76	0.82	1.45	0.62	0.39
21	3.66	3.58	2.72	93.8	3.67	3.28	0.43	0.11	1.09	0.20	2.46	0.98	2.13	1.01	0.42

S.3 RobB	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.67	3.59	2.29	94.5	3.68	3.15	0.12	0.05	0.82	0.15	2.26	1.03	1.84	0.91	0.40
2	3.68	3.60	2.26	94.5	3.69	2.96	0.05	0.03	0.83	0.15	2.03	0.90	1.48	0.68	0.39
3	3.66	3.59	2.31	94.1	3.68	3.24	0.21	0.08	0.82	0.15	2.50	1.12	2.21	1.09	0.41
4	3.67	3.59	2.36	94.2	3.68	3.16	0.16	0.06	0.82	0.15	2.48	1.22	1.66	0.76	0.40
5	3.68	3.60	2.33	94.3	3.69	2.98	0.06	0.03	0.83	0.15	2.32	1.09	1.27	0.55	0.39
6	3.66	3.58	2.35	93.6	3.68	3.25	0.26	0.09	0.82	0.15	2.71	1.32	1.93	0.92	0.41
7	3.67	3.59	2.16	93.3	3.69	3.11	0.12	0.05	0.82	0.15	2.01	0.84	2.09	1.08	0.40
8	3.68	3.60	2.16	93.3	3.69	2.92	0.05	0.03	0.83	0.15	1.74	0.73	1.68	0.82	0.39
9	3.66	3.59	2.20	92.7	3.68	3.21	0.22	0.08	0.82	0.15	2.25	0.93	2.35	1.26	0.41
10	3.68	3.59	2.36	94.6	3.69	3.18	0.13	0.06	0.84	0.16	2.37	1.05	1.87	0.91	0.40
11	3.69	3.60	2.31	94.6	3.70	3.00	0.06	0.03	0.85	0.16	2.01	0.94	1.44	0.68	0.39
12	3.67	3.59	2.38	94.2	3.68	3.27	0.23	0.09	0.84	0.16	2.60	1.14	2.21	1.07	0.41
13	3.67	3.59	2.22	94.2	3.68	3.10	0.13	0.05	0.80	0.14	2.12	1.00	1.85	0.92	0.40
14	3.68	3.60	2.20	94.1	3.68	2.91	0.06	0.03	0.81	0.15	2.06	0.87	1.48	0.68	0.39
15	3.65	3.58	2.23	93.6	3.68	3.20	0.19	0.08	0.80	0.14	2.44	1.10	2.14	1.10	0.41
16	3.68	3.60	1.83	92.6	3.69	3.20	0.15	0.07	0.60	0.11	2.53	1.18	2.07	1.05	0.40
17	3.69	3.60	1.81	92.6	3.70	3.01	0.07	0.04	0.61	0.11	2.32	1.04	1.74	0.79	0.39
18	3.67	3.59	1.85	92.3	3.69	3.29	0.26	0.10	0.60	0.11	2.79	1.29	2.42	1.24	0.41
19	3.67	3.59	2.72	94.9	3.68	3.09	0.10	0.04	1.10	0.20	1.94	0.88	1.62	0.78	0.40
20	3.68	3.60	2.69	95.1	3.69	2.89	0.04	0.02	1.10	0.20	1.73	0.77	1.25	0.58	0.39
21	3.66	3.58	2.73	94.2	3.68	3.18	0.16	0.07	1.10	0.20	2.25	0.96	1.91	0.94	0.41
S.4 RSL	GTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.51	5.38	1.58	72.6	5.46	2.23	0.04	0.02	0.74	0.13	2.40	0.79	2.08	0.90	0.58
2	5.53	5.37	1.38	69.8	5.49	2.08	0.02	0.01	0.68	0.13	2.14	0.66	1.99	0.73	0.56
3	5.51	5.37	1.79	74.5	5.43	2.38	0.06	0.03	0.82	0.15	2.42	0.90	2.27	1.04	0.60
4	5.52	5.38	1.60	73.3	5.46	2.28	0.04	0.02	0.77	0.14	2.64	0.93	1.83	0.76	0.58
5	5.54	5.37	1.40	70.1	5.50	2.13	0.02	0.01	0.70	0.13	2.47	0.78	1.76	0.60	0.56
6	5.52	5.38	1.81	75.1	5.42	2.43	0.06	0.03	0.84	0.15	2.69	1.05	2.05	0.88	0.60
7	5.52	5.38	1.63	71.1	5.46	2.21	0.05	0.02	0.76	0.13	2.12	0.68	2.35	1.06	0.58
8	5.53	5.37	1.39	68.8	5.48	2.06	0.03	0.01	0.69	0.12	2.02	0.56	2.20	0.86	0.56
9	5.51	5.37	1.78	73.1	5.44	2.36	0.06	0.03	0.80	0.15	2.16	0.77	2.44	1.21	0.60
10	5.52	5.38	1.65	73.6	5.45	2.27	0.04	0.02	0.74	0.13	2.42	0.82	2.08	0.92	0.58
11	5.54	5.37	1.42	70.8	5.48	2.11	0.02	0.01	0.69	0.12	2.27	0.68	1.99	0.75	0.56
12	5.52	5.37	1.82	75.3	5.42	2.42	0.06	0.03	0.83	0.15	2.44	0.92	2.30	1.06	0.60
13	5.50	5.38	1.56	71.2	5.47	2.20	0.04	0.02	0.78	0.14	2.37	0.78	2.11	0.88	0.58
14	5.52	5.37	1.36	68.9	5.50	2.06	0.02	0.01	0.69	0.13	2.10	0.65	2.00	0.70	0.56
15	5.51	5.37	1.78	73.5	5.44	2.34	0.06	0.03	0.82	0.15	2.40	0.88	2.24	1.02	0.60
16	5.52	5.37	1.29	70.2	5.48	2.37	0.06	0.02	0.51	0.09	2.91	0.99	2.60	1.10	0.58
17	5.54	5.36	1.16	68.0	5.51	2.24	0.03	0.01	0.48	0.09	2.59	0.83	2.44	0.89	0.56
18	5.53	5.37	1.36	72.0	5.44	2.50	0.08	0.03	0.57	0.10	2.95	1.11	2.88	1.26	0.60
19	5.50	5.37	1.86	72.8	5.42	2.10	0.03	0.01	1.06	0.20	1.95	0.63	1.62	0.72	0.58
20	5.51	5.37	1.46	70.2	5.43	1.93	0.02	0.01	0.96	0.18	1.76	0.53	1.60	0.58	0.56
21	5.51	5.37	2.05	75.2	5.41	2.27	0.05	0.02	1.13	0.22	1.98	0.72	1.81	0.83	0.60

S.4 2mm	GTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.50	5.37	1.52	72.0	5.46	2.18	0.04	0.02	0.73	0.13	1.40	0.46	2.08	0.84	0.52
2	5.51	5.36	1.31	68.9	5.48	2.04	0.02	0.01	0.67	0.12	1.24	0.39	2.01	0.68	0.51
3	5.49	5.36	1.67	73.8	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.53	2.17	0.97	0.53
4	5.51	5.37	1.53	73.3	5.46	2.24	0.04	0.02	0.76	0.13	1.64	0.55	1.84	0.70	0.52
5	5.52	5.36	1.35	69.5	5.49	2.10	0.02	0.01	0.69	0.12	1.46	0.47	1.79	0.56	0.51
6	5.51	5.37	1.70	75.5	5.44	2.37	0.06	0.03	0.87	0.15	1.76	0.63	1.91	0.82	0.53
7	5.50	5.36	1.49	70.3	5.46	2.13	0.04	0.02	0.71	0.13	1.20	0.39	2.32	0.99	0.52
8	5.52	5.36	1.27	67.6	5.46	2.00	0.02	0.01	0.65	0.12	1.06	0.33	2.23	0.81	0.51
9	5.49	5.36	1.64	71.9	5.44	2.26	0.06	0.03	0.81	0.14	1.26	0.44	2.40	1.13	0.53
10	5.51	5.38	1.54	72.9	5.45	2.21	0.04	0.02	0.73	0.13	1.43	0.48	2.06	0.86	0.52
11	5.52	5.37	1.35	70.0	5.47	2.07	0.02	0.01	0.68	0.12	1.32	0.41	2.01	0.70	0.51
12	5.50	5.37	1.72	74.8	5.43	2.35	0.06	0.03	0.85	0.14	1.51	0.54	2.18	0.99	0.53
13	5.49	5.37	1.49	70.8	5.47	2.15	0.04	0.02	0.73	0.13	1.40	0.45	2.11	0.82	0.52
14	5.51	5.36	1.25	68.0	5.48	2.02	0.02	0.01	0.67	0.12	1.23	0.38	2.02	0.66	0.51
15	5.49	5.36	1.65	72.9	5.45	2.27	0.06	0.03	0.84	0.14	1.44	0.51	2.16	0.95	0.53
16	5.51	5.36	1.17	69.9	5.47	2.32	0.05	0.02	0.50	0.09	1.66	0.58	2.51	1.02	0.52
17	5.52	5.35	1.08	67.4	5.49	2.20	0.03	0.01	0.47	0.08	1.49	0.49	2.41	0.83	0.51
18	5.50	5.36	1.32	72.1	5.44	2.43	0.08	0.03	0.56	0.10	1.77	0.65	2.63	1.17	0.53
19	5.48	5.36	1.73	72.1	5.42	2.04	0.03	0.01	1.03	0.19	1.17	0.37	1.69	0.68	0.52
20	5.49	5.36	1.30	69.2	5.44	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.65	0.54	0.51
21	5.48	5.35	1.94	74.3	5.40	2.19	0.05	0.02	1.16	0.21	1.22	0.42	1.74	0.78	0.53
S.4 BS	GTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.50	5.37	1.50	72.4	5.46	2.18	0.04	0.02	0.73	0.13	1.36	0.46	1.99	0.80	0.52
2	5.52	5.37	1.31	69.3	5.49	2.05	0.02	0.01	0.66	0.12	1.24	0.39	1.92	0.65	0.50
3	5.49	5.36	1.65	74.0	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.52	2.10	0.93	0.53
4	5.51	5.37	1.53	73.6	5.47	2.24	0.04	0.02	0.76	0.13	1.60	0.55	1.75	0.67	0.52
5	5.53	5.36	1.35	69.6	5.50	2.11	0.02	0.01	0.69	0.12	1.46	0.46	1.69	0.53	0.50
6	5.51	5.36	1.71	75.7	5.45	2.37	0.06	0.03	0.88	0.15	1.62	0.62	1.82	0.78	0.53
7	5.50	5.36	1.47	70.2	5.46	2.14	0.05	0.02	0.70	0.13	1.19	0.39	2.24	0.95	0.52
8	5.53	5.36	1.26	67.7	5.48	2.00	0.03	0.01	0.65	0.12	1.07	0.33	2.15	0.77	0.50
9	5.49	5.35	1.62	72.0	5.45	2.26	0.06	0.03	0.78	0.14	1.21	0.44	2.33	1.08	0.53
10	5.51	5.37	1.52	73.1	5.46	2.21	0.04	0.02	0.73	0.13	1.38	0.48	1.97	0.82	0.52
11	5.54	5.37	1.34	70.3	5.48	2.08	0.02	0.01	0.68	0.12	1.32	0.41	1.91	0.67	0.50
12	5.51	5.37	1.72	75.1	5.44	2.35	0.06	0.03	0.81	0.14	1.45	0.54	2.00	0.95	0.53
13	5.50	5.36	1.47	71.0	5.48	2.15	0.04	0.02	0.73	0.13	1.37	0.45	2.02	0.79	0.52
14	5.52	5.37	1.26	68.1	5.49	2.03	0.02	0.01	0.66	0.12	1.19	0.38	1.94	0.63	0.50
15	5.49	5.36	1.62	72.9	5.45	2.28	0.06	0.03	0.84	0.14	1.44	0.51	2.09	0.91	0.53
16	5.51	5.36	1.17	70.4	5.48	2.32	0.06	0.02	0.50	0.09	1.64	0.58	2.42	0.98	0.52
17	5.53	5.35	1.07	67.6	5.50	2.21	0.03	0.02	0.47	0.08	1.49	0.49	2.31	0.80	0.50
18	5.51	5.36	1.30	72.3	5.45	2.44	0.08	0.03	0.55	0.10	1.72	0.65	2.54	1.13	0.53
19	5.49	5.36	1.71	72.2	5.42	2.04	0.03	0.01	1.02	0.19	1.13	0.37	1.62	0.64	0.52
20	5.50	5.36	1.29	69.3	5.45	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.57	0.51	0.50
21	5.48	5.35	1.94	74.3	5.41	2.19	0.05	0.02	1.16	0.21	1.21	0.42	1.67	0.74	0.53

S.4 2mm	GTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.50	5.37	1.52	72.0	5.46	2.18	0.04	0.02	0.73	0.13	1.40	0.46	2.08	0.84	0.52
2	5.51	5.36	1.31	68.9	5.48	2.04	0.02	0.01	0.67	0.12	1.24	0.39	2.01	0.68	0.51
3	5.49	5.36	1.67	73.8	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.53	2.17	0.97	0.53
4	5.51	5.37	1.53	73.3	5.46	2.24	0.04	0.02	0.76	0.13	1.64	0.55	1.84	0.70	0.52
5	5.52	5.36	1.35	69.5	5.49	2.10	0.02	0.01	0.69	0.12	1.46	0.47	1.79	0.56	0.51
6	5.51	5.37	1.70	75.5	5.44	2.37	0.06	0.03	0.87	0.15	1.76	0.63	1.91	0.82	0.53
7	5.50	5.36	1.49	70.3	5.46	2.13	0.04	0.02	0.71	0.13	1.20	0.39	2.32	0.99	0.52
8	5.52	5.36	1.27	67.6	5.46	2.00	0.02	0.01	0.65	0.12	1.06	0.33	2.23	0.81	0.51
9	5.49	5.36	1.64	71.9	5.44	2.26	0.06	0.03	0.81	0.14	1.26	0.44	2.40	1.13	0.53
10	5.51	5.38	1.54	72.9	5.45	2.21	0.04	0.02	0.73	0.13	1.43	0.48	2.06	0.86	0.52
11	5.52	5.37	1.35	70.0	5.47	2.07	0.02	0.01	0.68	0.12	1.32	0.41	2.01	0.70	0.51
12	5.50	5.37	1.72	74.8	5.43	2.35	0.06	0.03	0.85	0.14	1.51	0.54	2.18	0.99	0.53
13	5.49	5.37	1.49	70.8	5.47	2.15	0.04	0.02	0.73	0.13	1.40	0.45	2.11	0.82	0.52
14	5.51	5.36	1.25	68.0	5.48	2.02	0.02	0.01	0.67	0.12	1.23	0.38	2.02	0.66	0.51
15	5.49	5.36	1.65	72.9	5.45	2.27	0.06	0.03	0.84	0.14	1.44	0.51	2.16	0.95	0.53
16	5.51	5.36	1.17	69.9	5.47	2.32	0.05	0.02	0.50	0.09	1.66	0.58	2.51	1.02	0.52
17	5.52	5.35	1.08	67.4	5.49	2.20	0.03	0.01	0.47	0.08	1.49	0.49	2.41	0.83	0.51
18	5.50	5.36	1.32	72.1	5.44	2.43	0.08	0.03	0.56	0.10	1.77	0.65	2.63	1.17	0.53
19	5.48	5.36	1.73	72.1	5.42	2.04	0.03	0.01	1.03	0.19	1.17	0.37	1.69	0.68	0.52
20	5.49	5.36	1.30	69.2	5.44	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.65	0.54	0.51
21	5.48	5.35	1.94	74.3	5.40	2.19	0.05	0.02	1.16	0.21	1.22	0.42	1.74	0.78	0.53
S.4 BS	GTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.50	5.37	1.50	72.4	5.46	2.18	0.04	0.02	0.73	0.13	1.36	0.46	1.99	0.80	0.52
2	5.52	5.37	1.31	69.3	5.49	2.05	0.02	0.01	0.66	0.12	1.24	0.39	1.92	0.65	0.50
3	5.49	5.36	1.65	74.0	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.52	2.10	0.93	0.53
4	5.51	5.37	1.53	73.6	5.47	2.24	0.04	0.02	0.76	0.13	1.60	0.55	1.75	0.67	0.52
5	5.53	5.36	1.35	69.6	5.50	2.11	0.02	0.01	0.69	0.12	1.46	0.46	1.69	0.53	0.50
6	5.51	5.36	1.71	75.7	5.45	2.37	0.06	0.03	0.88	0.15	1.62	0.62	1.82	0.78	0.53
7	5.50	5.36	1.47	70.2	5.46	2.14	0.05	0.02	0.70	0.13	1.19	0.39	2.24	0.95	0.52
8	5.53	5.36	1.26	67.7	5.48	2.00	0.03	0.01	0.65	0.12	1.07	0.33	2.15	0.77	0.50
9	5.49	5.35	1.62	72.0	5.45	2.26	0.06	0.03	0.78	0.14	1.21	0.44	2.33	1.08	0.53
10	5.51	5.37	1.52	73.1	5.46	2.21	0.04	0.02	0.73	0.13	1.38	0.48	1.97	0.82	0.52
11	5.54	5.37	1.34	70.3	5.48	2.08	0.02	0.01	0.68	0.12	1.32	0.41	1.91	0.67	0.50
12	5.51	5.37	1.72	75.1	5.44	2.35	0.06	0.03	0.81	0.14	1.45	0.54	2.00	0.95	0.53
13	5.50	5.36	1.47	71.0	5.48	2.15	0.04	0.02	0.73	0.13	1.37	0.45	2.02	0.79	0.52
14	5.52	5.37	1.26	68.1	5.49	2.03	0.02	0.01	0.66	0.12	1.19	0.38	1.94	0.63	0.50
15	5.49	5.36	1.62	72.9	5.45	2.28	0.06	0.03	0.84	0.14	1.44	0.51	2.09	0.91	0.53
16	5.51	5.36	1.17	70.4	5.48	2.32	0.06	0.02	0.50	0.09	1.64	0.58	2.42	0.98	0.52
17	5.53	5.35	1.07	67.6	5.50	2.21	0.03	0.02	0.47	0.08	1.49	0.49	2.31	0.80	0.50
18	5.51	5.36	1.30	72.3	5.45	2.44	0.08	0.03	0.55	0.10	1.72	0.65	2.54	1.13	0.53
19	5.49	5.36	1.71	72.2	5.42	2.04	0.03	0.01	1.02	0.19	1.13	0.37	1.62	0.64	0.52
20	5.50	5.36	1.29	69.3	5.45	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.57	0.51	0.50
21	5.48	5.35	1.94	74.3	5.41	2.19	0.05	0.02	1.16	0.21	1.21	0.42	1.67	0.74	0.53

S.4 RobA	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.50	5.37	1.50	72.4	5.46	2.18	0.04	0.02	0.73	0.13	1.36	0.46	1.99	0.80	0.52
2	5.52	5.37	1.31	69.3	5.49	2.05	0.02	0.01	0.66	0.12	1.24	0.39	1.92	0.65	0.50
3	5.49	5.36	1.65	74.0	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.52	2.10	0.93	0.53
4	5.51	5.37	1.53	73.6	5.47	2.24	0.04	0.02	0.76	0.13	1.60	0.55	1.75	0.67	0.52
5	5.53	5.36	1.35	69.6	5.50	2.11	0.02	0.01	0.69	0.12	1.46	0.46	1.69	0.53	0.50
6	5.51	5.36	1.71	75.7	5.45	2.37	0.06	0.03	0.88	0.15	1.62	0.62	1.82	0.78	0.53
7	5.50	5.36	1.47	70.2	5.46	2.14	0.05	0.02	0.70	0.13	1.19	0.39	2.24	0.95	0.52
8	5.53	5.36	1.26	67.7	5.48	2.00	0.03	0.01	0.65	0.12	1.07	0.33	2.15	0.77	0.50
9	5.49	5.35	1.62	72.0	5.45	2.26	0.06	0.03	0.78	0.14	1.21	0.44	2.33	1.08	0.53
10	5.51	5.37	1.52	73.1	5.46	2.21	0.04	0.02	0.73	0.13	1.38	0.48	1.97	0.82	0.52
11	5.54	5.37	1.34	70.3	5.48	2.08	0.02	0.01	0.68	0.12	1.32	0.41	1.91	0.67	0.50
12	5.51	5.37	1.72	75.1	5.44	2.35	0.06	0.03	0.81	0.14	1.45	0.54	2.00	0.95	0.53
13	5.50	5.36	1.47	71.0	5.48	2.15	0.04	0.02	0.73	0.13	1.37	0.45	2.02	0.79	0.52
14	5.52	5.37	1.26	68.1	5.49	2.03	0.02	0.01	0.66	0.12	1.19	0.38	1.94	0.63	0.50
15	5.49	5.36	1.62	72.9	5.45	2.28	0.06	0.03	0.84	0.14	1.44	0.51	2.09	0.91	0.53
16	5.51	5.36	1.17	70.4	5.48	2.32	0.06	0.02	0.50	0.09	1.64	0.58	2.42	0.98	0.52
17	5.53	5.35	1.07	67.6	5.50	2.21	0.03	0.02	0.47	0.08	1.49	0.49	2.31	0.80	0.50
18	5.51	5.36	1.30	72.3	5.45	2.44	0.08	0.03	0.55	0.10	1.72	0.65	2.54	1.13	0.53
19	5.49	5.36	1.71	72.2	5.42	2.04	0.03	0.01	1.02	0.19	1.13	0.37	1.62	0.64	0.52
20	5.50	5.36	1.29	69.3	5.45	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.57	0.51	0.50
21	5.48	5.35	1.94	74.3	5.41	2.19	0.05	0.02	1.16	0.21	1.21	0.42	1.67	0.74	0.53
S.4 RobB	CTV				Br.		Ch.		SC		L. Hip.		R. Hip.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.5	5.37	1.5	72.4	5.46	2.18	0.04	0.02	0.73	0.13	1.36	0.46	1.99	0.8	0.52
2	5.52	5.37	1.31	69.3	5.49	2.05	0.02	0.01	0.66	0.12	1.24	0.39	1.92	0.65	0.5
3	5.49	5.36	1.65	74	5.45	2.31	0.06	0.03	0.85	0.14	1.48	0.52	2.1	0.93	0.53
4	5.51	5.37	1.53	73.6	5.47	2.24	0.04	0.02	0.76	0.13	1.6	0.55	1.75	0.67	0.52
5	5.53	5.36	1.35	69.6	5.5	2.11	0.02	0.01	0.69	0.12	1.46	0.46	1.69	0.53	0.5
6	5.51	5.36	1.71	75.7	5.45	2.37	0.06	0.03	0.88	0.15	1.62	0.62	1.82	0.78	0.53
7	5.5	5.36	1.47	70.2	5.46	2.14	0.05	0.02	0.7	0.13	1.19	0.39	2.24	0.95	0.52
8	5.53	5.36	1.26	67.7	5.48	2	0.03	0.01	0.65	0.12	1.07	0.33	2.15	0.77	0.5
9	5.49	5.35	1.62	72	5.45	2.26	0.06	0.03	0.78	0.14	1.21	0.44	2.33	1.08	0.53
10	5.51	5.37	1.52	73.1	5.46	2.21	0.04	0.02	0.73	0.13	1.38	0.48	1.97	0.82	0.52
11	5.54	5.37	1.34	70.3	5.48	2.08	0.02	0.01	0.68	0.12	1.32	0.41	1.91	0.67	0.5
12	5.51	5.37	1.72	75.1	5.44	2.35	0.06	0.03	0.81	0.14	1.45	0.54	2	0.95	0.53
13	5.5	5.36	1.47	71	5.48	2.15	0.04	0.02	0.73	0.13	1.37	0.45	2.02	0.79	0.52
14	5.52	5.37	1.26	68.1	5.49	2.03	0.02	0.01	0.66	0.12	1.19	0.38	1.94	0.63	0.5
15	5.49	5.36	1.62	72.9	5.45	2.28	0.06	0.03	0.84	0.14	1.44	0.51	2.09	0.91	0.53
16	5.51	5.36	1.17	70.4	5.48	2.32	0.06	0.02	0.5	0.09	1.64	0.58	2.42	0.98	0.52
17	5.53	5.35	1.07	67.6	5.5	2.21	0.03	0.02	0.47	0.08	1.49	0.49	2.31	0.8	0.5
18	5.51	5.36	1.3	72.3	5.45	2.44	0.08	0.03	0.55	0.1	1.72	0.65	2.54	1.13	0.53
19	5.49	5.36	1.71	72.2	5.42	2.04	0.03	0.01	1.02	0.19	1.13	0.37	1.62	0.64	0.52
20	5.5	5.36	1.29	69.3	5.45	1.89	0.02	0.01	0.95	0.17	1.05	0.31	1.57	0.51	0.5
21	5.48	5.35	1.94	74.3	5.41	2.19	0.05	0.02	1.16	0.21	1.21	0.42	1.67	0.74	0.53

Patient BK007															
S.1 RSL	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.1	30.6	30.4	100.0	30.6	24.1	4.7	1.1	31.5	17.2	19.1	13.3	20.0	11.2	7.4
2	31.1	30.6	30.2	100.0	30.8	24.1	4.3	1.1	31.6	16.5	17.5	12.5	18.1	10.4	7.2
3	31.1	30.6	30.3	100.0	30.5	24.2	5.0	1.1	31.4	17.8	21.0	14.7	21.7	12.6	7.6
4	31.1	30.6	30.3	100.0	30.7	24.2	3.9	1.1	31.5	17.2	20.0	14.2	18.8	10.4	7.4
5	31.1	30.6	30.2	100.0	30.8	24.2	3.6	1.1	31.6	16.6	18.3	13.3	16.8	9.5	7.2
6	31.1	30.6	30.3	100.0	30.5	24.3	4.0	1.1	31.4	17.8	21.7	15.4	20.4	11.7	7.6
7	31.1	30.6	30.3	100.0	30.6	24.2	4.8	1.1	31.4	17.2	18.6	12.7	21.2	12.3	7.4
8	31.1	30.6	30.0	99.9	30.8	24.1	4.6	1.1	31.5	16.5	16.9	11.8	19.1	11.3	7.2
9	31.1	30.6	30.3	100.0	30.6	24.2	5.0	1.1	31.3	17.8	20.3	13.9	22.8	13.5	7.6
10	31.2	30.6	30.2	99.9	30.8	25.6	6.0	1.6	31.2	17.1	21.3	15.8	22.1	13.4	7.5
11	31.1	30.6	29.6	99.2	30.8	25.6	5.8	1.6	31.3	16.4	19.7	14.9	20.3	12.5	7.3
12	31.3	30.6	30.3	100.0	30.7	25.6	7.2	1.6	31.1	17.7	23.0	17.0	23.5	14.5	7.7
13	31.1	30.6	30.2	100.0	30.5	22.5	3.1	0.8	31.6	17.3	17.0	11.1	18.2	9.5	7.3
14	31.1	30.6	30.0	100.0	30.6	22.5	2.5	0.7	31.6	16.7	15.1	10.2	16.0	8.4	7.1
15	31.0	30.5	30.2	100.0	30.4	22.6	3.3	0.8	31.5	18.0	18.8	12.4	19.8	10.8	7.5
16	31.2	30.6	30.3	100.0	30.7	24.7	5.0	1.2	31.4	16.6	19.0	13.3	20.3	11.5	7.5
17	31.2	30.6	30.0	100.0	30.9	24.7	4.1	1.1	31.6	16.0	17.4	12.5	18.3	10.5	7.3
18	31.3	30.6	30.3	100.0	30.6	24.8	5.4	1.2	31.4	17.2	20.6	14.4	21.9	12.7	7.6
19	31.1	30.6	30.3	100.0	30.6	23.5	4.3	1.0	31.5	17.8	19.6	13.7	20.0	11.3	7.4
20	31.1	30.6	30.0	100.0	30.7	23.5	4.1	1.0	31.6	17.1	17.8	12.7	18.0	10.3	7.2
21	31.0	30.6	30.3	100.0	30.5	23.6	4.6	1.0	31.3	18.4	21.3	15.0	21.6	12.5	7.5
S.1 2mm	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.9	30.6	29.6	99.7	30.2	21.0	3.7	0.7	31.2	16.7	16.1	11.1	19.3	10.2	6.8
2	31.8	30.7	29.5	99.2	30.4	21.0	3.5	0.7	31.1	16.1	15.5	10.2	17.9	9.4	6.6
3	31.9	30.6	29.6	99.7	30.0	21.2	3.9	0.8	31.1	17.4	16.9	11.7	20.1	11.1	7.0
4	31.9	30.6	29.6	99.7	30.2	21.1	3.7	0.7	31.2	16.8	16.9	11.8	18.1	9.6	6.8
5	31.8	30.7	29.6	99.4	30.4	21.0	3.3	0.7	31.1	16.1	16.4	11.0	16.7	8.6	6.6
6	32.0	30.6	29.6	99.7	30.1	21.2	3.9	0.7	31.1	17.4	17.7	12.3	19.0	10.4	7.0
7	31.9	30.6	29.5	99.3	30.2	21.1	3.8	0.8	31.1	16.8	15.3	10.6	20.5	11.1	6.8
8	31.8	30.7	29.3	98.8	30.4	21.0	3.6	0.8	31.1	16.1	14.7	9.6	19.1	10.2	6.6
9	31.9	30.6	29.5	99.4	30.1	21.2	3.9	0.8	31.0	17.4	16.2	11.1	21.3	11.8	7.0
10	32.0	30.6	29.2	98.3	30.5	22.8	5.7	1.2	31.0	16.7	18.5	13.3	21.5	12.1	6.9
11	31.9	30.7	28.9	97.6	30.6	22.7	5.3	1.1	31.0	16.0	17.8	12.2	20.0	11.1	6.7
12	32.1	30.6	29.3	98.7	30.4	22.9	5.9	1.2	31.1	17.3	19.4	14.0	22.2	13.1	7.0
13	31.7	30.6	29.6	99.6	29.7	19.3	2.3	0.5	31.5	16.9	13.6	9.0	16.9	8.5	6.7
14	31.6	30.7	29.6	99.5	30.0	19.1	2.2	0.5	31.4	16.2	12.9	8.4	15.7	7.7	6.5
15	31.7	30.6	29.5	99.6	29.6	19.5	2.4	0.5	31.3	17.5	14.5	9.5	17.6	9.2	6.8
16	32.0	30.6	29.6	99.6	30.2	21.6	3.9	0.8	31.1	16.3	15.7	10.8	19.5	10.4	6.9
17	31.9	30.7	29.4	98.9	30.4	21.5	3.7	0.7	31.2	15.6	15.2	10.1	18.1	9.5	6.7
18	32.0	30.6	29.5	99.6	30.1	21.8	4.1	0.8	31.1	16.9	16.5	11.4	20.2	11.2	7.0
19	31.7	30.6	29.6	99.7	30.2	20.4	3.6	0.7	31.2	17.3	16.6	11.5	19.2	10.2	6.8
20	31.7	30.7	29.4	99.0	30.3	20.3	3.3	0.7	31.2	16.6	15.8	10.6	17.7	9.2	6.6
21	31.7	30.6	29.5	99.6	30.0	20.6	3.7	0.7	31.1	17.9	17.3	12.0	20.1	11.0	6.9

S.1 BS	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.1	30.7	30.4	100.0	30.3	21.6	4.2	1.1	31.2	17.6	18.2	12.7	19.6	11.1	7.0
2	31.2	30.7	30.3	100.0	30.5	21.5	4.1	1.1	31.3	16.9	16.7	11.8	18.2	10.3	6.8
3	31.2	30.7	30.2	100.0	30.1	21.8	4.7	1.1	31.1	18.3	19.5	13.8	20.6	12.2	7.1
4	31.2	30.7	30.3	100.0	30.3	21.7	4.1	1.0	31.2	17.7	19.1	13.5	18.5	10.6	7.0
5	31.2	30.7	30.3	100.0	30.5	21.6	4.0	1.0	31.3	16.9	17.4	12.5	17.1	9.6	6.8
6	31.2	30.7	30.1	99.9	30.2	21.9	4.3	1.1	31.2	18.4	20.2	14.5	19.5	11.5	7.1
7	31.1	30.7	30.3	100.0	30.3	21.7	4.4	1.1	31.1	17.6	17.6	12.1	20.7	12.0	7.0
8	31.2	30.7	30.1	99.8	30.5	21.5	4.3	1.1	31.2	16.9	16.0	11.1	19.3	11.0	6.8
9	31.1	30.7	30.2	100.0	30.2	21.8	4.8	1.1	31.1	18.3	18.7	13.1	21.7	12.9	7.1
10	31.3	30.7	30.0	99.8	30.6	23.2	6.1	1.6	30.9	17.6	20.4	14.9	21.6	13.3	7.1
11	31.3	30.7	29.6	99.3	30.7	23.2	5.9	1.6	30.9	16.9	18.9	13.9	20.3	12.3	6.9
12	31.3	30.6	30.1	99.9	30.5	23.4	6.4	1.6	30.8	18.2	21.6	16.0	22.5	14.2	7.2
13	31.0	30.7	30.2	99.8	29.9	20.0	3.1	0.7	31.4	17.8	16.1	10.7	17.6	9.4	6.9
14	31.1	30.7	30.2	99.9	30.1	19.9	2.7	0.7	31.4	17.0	14.4	9.7	16.0	8.4	6.7
15	31.0	30.6	29.9	99.6	29.8	20.2	3.2	0.7	31.3	18.5	17.2	11.7	18.5	10.3	7.0
16	31.2	30.7	30.3	100.0	30.4	22.2	4.8	1.1	31.2	17.1	17.9	12.4	19.7	11.3	7.0
17	31.3	30.7	30.2	99.9	30.6	22.1	4.3	1.1	31.3	16.3	16.3	11.5	18.3	10.3	6.8
18	31.3	30.6	30.3	100.0	30.2	22.4	5.0	1.1	31.1	17.8	19.1	13.4	20.7	12.2	7.2
19	31.1	30.7	30.2	100.0	30.2	21.0	4.1	1.0	31.2	18.3	18.7	13.2	19.6	11.2	7.0
20	31.1	30.7	30.2	100.0	30.4	20.9	4.0	1.0	31.3	17.5	17.0	12.1	18.2	10.2	6.8
21	31.1	30.6	30.0	99.9	30.1	21.2	4.2	1.1	31.1	18.9	19.8	14.3	20.5	12.1	7.1
S.1 RobA	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.9	30.9	29.6	99.5	30.3	18.9	1.9	0.5	30.2	14.6	15.6	10.1	19.1	9.5	6.4
2	31.9	30.9	29.7	99.6	30.4	18.8	1.7	0.4	30.2	13.8	14.6	9.5	17.4	8.7	6.2
3	31.9	30.8	29.6	99.6	30.2	19.0	2.3	0.5	30.3	15.4	17.0	10.8	20.2	10.4	6.5
4	31.9	30.9	29.6	99.7	30.4	19.0	2.0	0.5	30.3	14.6	16.4	10.8	17.9	8.8	6.4
5	31.9	30.9	29.7	99.6	30.4	19.0	1.8	0.4	30.3	13.9	15.3	10.1	16.1	7.9	6.2
6	31.9	30.8	29.6	99.6	30.3	19.1	2.2	0.5	30.4	15.4	17.8	11.4	18.9	9.7	6.5
7	31.9	30.9	29.5	99.3	30.3	18.8	2.1	0.5	30.4	14.6	14.9	9.7	20.5	10.5	6.4
8	31.8	30.9	29.5	99.2	30.4	18.8	1.6	0.4	30.4	13.9	13.9	8.9	18.7	9.6	6.2
9	31.8	30.8	29.5	99.3	30.2	18.9	2.4	0.5	30.4	15.4	16.3	10.3	21.5	11.3	6.5
10	32.0	30.9	29.2	98.4	30.7	21.3	3.0	0.7	31.0	15.6	18.3	12.5	21.4	11.5	6.4
11	32.0	30.9	29.2	98.1	30.7	21.3	2.6	0.6	31.0	14.9	17.1	11.6	19.6	10.6	6.3
12	32.0	30.8	29.3	98.6	30.6	21.3	3.2	0.7	31.1	16.3	19.6	13.3	22.2	12.4	6.6
13	31.8	30.9	29.5	99.3	29.5	16.4	1.4	0.3	29.0	13.4	13.0	8.0	16.7	7.8	6.3
14	31.7	30.9	29.5	99.3	29.6	16.3	1.1	0.3	28.9	12.6	11.8	7.5	15.1	7.0	6.1
15	31.7	30.8	29.4	99.3	29.4	16.6	1.6	0.3	29.1	14.1	14.5	8.7	17.6	8.4	6.4
16	31.9	30.9	29.6	99.3	30.4	19.4	2.1	0.5	30.2	14.0	15.2	9.9	19.4	9.7	6.4
17	31.9	30.9	29.7	99.4	30.4	19.4	1.8	0.5	30.2	13.3	14.2	9.3	17.5	8.8	6.2
18	31.9	30.8	29.5	99.4	30.3	19.5	2.6	0.5	30.3	14.8	16.5	10.5	20.2	10.5	6.5
19	31.8	30.9	29.6	99.5	30.3	18.2	1.8	0.4	30.4	15.2	16.4	10.6	19.1	9.5	6.3
20	31.8	30.9	29.6	99.5	30.3	18.2	1.4	0.4	30.3	14.5	14.9	9.8	17.2	8.6	6.2
21	31.8	30.8	29.6	99.4	30.1	18.4	1.9	0.5	30.5	16.0	17.6	11.3	20.3	10.3	6.4

S.1 RobB	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	31.7	30.6	29.4	99.2	30.1	18.7	1.9	0.5	30.0	14.5	15.5	10.1	19.0	9.4	6.3
2	31.7	30.7	29.5	99.2	30.2	18.7	1.7	0.4	30.0	13.7	14.5	9.4	17.3	8.7	6.1
3	31.7	30.6	29.4	99.3	30.0	18.8	2.3	0.5	30.1	15.3	16.9	10.8	20.1	10.3	6.4
4	31.7	30.6	29.4	99.3	30.2	18.9	2.0	0.4	30.1	14.5	16.3	10.7	17.8	8.8	6.3
5	31.7	30.7	29.5	99.3	30.1	18.8	1.7	0.4	30.1	13.8	15.2	10.0	16.0	7.9	6.1
6	31.7	30.6	29.4	99.3	30.0	19.0	2.2	0.5	30.2	15.3	17.7	11.3	18.8	9.6	6.4
7	31.6	30.6	29.3	98.9	30.1	18.7	2.1	0.5	30.2	14.5	14.8	9.6	20.4	10.4	6.3
8	31.6	30.7	29.3	98.8	30.1	18.6	1.6	0.4	30.1	13.8	13.8	8.9	18.6	9.6	6.1
9	31.6	30.6	29.3	98.8	30.0	18.8	2.4	0.5	30.2	15.3	16.2	10.3	21.4	11.2	6.4
10	31.8	30.7	29.1	97.9	30.4	21.1	3.0	0.7	30.7	15.5	18.2	12.5	21.3	11.4	6.4
11	31.8	30.7	29.0	97.8	30.5	21.1	2.6	0.6	30.7	14.8	17.0	11.5	19.5	10.6	6.2
12	31.7	30.6	29.1	98.2	30.4	21.1	3.1	0.7	30.8	16.2	19.5	13.2	22.1	12.3	6.5
13	31.5	30.6	29.3	98.9	29.3	16.3	1.4	0.3	28.8	13.3	13.0	8.0	16.7	7.7	6.2
14	31.5	30.7	29.3	98.8	29.4	16.1	1.1	0.3	28.7	12.5	11.8	7.5	15.0	7.0	6.1
15	31.5	30.6	29.2	98.7	29.2	16.4	1.6	0.3	28.8	14.0	14.5	8.6	17.5	8.4	6.3
16	31.7	30.7	29.4	98.8	30.1	19.3	2.1	0.5	30.0	13.9	15.1	9.9	19.3	9.6	6.4
17	31.7	30.7	29.4	99.1	30.2	19.2	1.8	0.5	30.0	13.2	14.1	9.2	17.4	8.8	6.2
18	31.7	30.6	29.3	99.1	30.0	19.4	2.5	0.5	30.0	14.7	16.4	10.5	20.1	10.4	6.5
19	31.6	30.6	29.4	99.1	30.0	18.1	1.8	0.4	30.1	15.1	16.3	10.5	19.0	9.4	6.3
20	31.5	30.7	29.4	99.2	30.1	18.0	1.4	0.4	30.1	14.4	14.9	9.7	17.1	8.5	6.1
21	31.5	30.6	29.4	99.0	29.9	18.2	1.9	0.5	30.3	15.9	17.5	11.2	20.1	10.3	6.4
S.2 RSL	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.4	19.8	19.5	99.5	19.7	10.8	0.5	0.1	19.0	7.1	10.5	6.7	12.9	5.4	3.7
2	20.5	19.8	19.5	99.5	19.4	9.3	0.4	0.1	18.6	6.8	8.7	5.8	9.9	4.0	3.6
3	20.4	19.8	19.5	99.6	19.8	12.0	0.6	0.2	19.4	7.4	13.0	8.1	15.3	7.3	3.8
4	20.4	19.8	19.5	99.4	19.8	11.0	0.4	0.1	19.1	7.2	13.2	9.0	11.0	4.2	3.7
5	20.5	19.8	19.5	99.4	19.4	9.4	0.3	0.1	18.6	6.9	10.9	7.7	7.7	2.8	3.6
6	20.4	19.8	19.5	99.5	19.9	12.1	0.5	0.1	19.5	7.5	15.3	10.3	13.3	5.7	3.8
7	20.4	19.8	19.5	99.5	19.7	10.9	0.6	0.1	19.0	7.1	8.5	5.1	14.8	7.3	3.7
8	20.5	19.8	19.5	99.4	19.4	9.3	0.5	0.1	18.5	6.8	6.8	4.3	11.7	5.5	3.6
9	20.4	19.8	19.5	99.5	19.9	12.0	0.7	0.2	19.4	7.4	10.6	6.1	16.8	9.1	3.8
10	20.5	19.8	19.5	99.5	19.8	11.5	0.6	0.2	19.2	7.2	11.1	7.2	13.5	6.0	3.7
11	20.5	19.8	19.5	99.5	19.6	9.9	0.4	0.1	18.7	7.0	9.1	6.3	10.3	4.4	3.6
12	20.5	19.8	19.5	99.6	19.9	12.6	0.7	0.2	19.5	7.5	13.3	8.3	15.7	7.7	3.8
13	20.3	19.8	19.5	99.5	19.6	10.3	0.4	0.1	18.9	7.0	10.7	6.6	12.8	5.3	3.7
14	20.4	19.8	19.5	99.4	19.1	8.8	0.3	0.1	18.4	6.7	8.3	5.4	9.5	3.7	3.6
15	20.3	19.8	19.5	99.6	19.7	11.5	0.5	0.1	19.4	7.4	13.0	7.8	15.0	7.0	3.8
16	20.5	19.8	19.4	99.2	19.7	11.2	0.6	0.2	18.3	6.3	10.3	6.5	12.1	5.2	3.7
17	20.6	19.8	19.4	99.0	19.3	9.6	0.4	0.1	17.7	6.1	8.4	5.5	9.1	3.8	3.6
18	20.5	19.8	19.5	99.2	19.8	12.3	0.7	0.2	18.9	6.6	12.5	7.6	14.6	6.7	3.8
19	20.3	19.8	19.5	99.7	19.8	10.5	0.4	0.1	19.4	7.9	11.8	7.4	13.7	6.2	3.7
20	20.4	19.8	19.5	99.6	19.5	9.0	0.3	0.1	19.0	7.6	9.3	6.2	10.6	4.5	3.6
21	20.3	19.8	19.5	99.7	19.8	11.7	0.4	0.1	19.8	8.2	14.0	8.7	15.7	8.0	3.8

S.2 2mm	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.4	19.8	19.5	99.5	19.6	10.3	0.4	0.1	18.7	6.6	9.0	5.5	11.8	4.7	3.5
2	20.4	19.8	19.5	99.4	19.2	8.8	0.3	0.1	18.2	6.3	7.3	4.7	8.9	3.4	3.4
3	20.4	19.8	19.5	99.5	19.7	11.5	0.5	0.1	19.2	7.0	11.3	6.7	14.2	6.5	3.6
4	20.4	19.8	19.4	99.4	19.6	10.5	0.4	0.1	18.9	6.7	11.5	7.6	10.0	3.5	3.5
5	20.4	19.8	19.4	99.2	19.3	8.9	0.3	0.1	18.3	6.4	9.4	6.4	6.8	2.3	3.4
6	20.4	19.8	19.4	99.5	19.7	11.6	0.4	0.1	19.2	7.1	13.7	8.8	12.2	4.9	3.6
7	20.4	19.8	19.4	99.4	19.6	10.4	0.5	0.1	18.8	6.7	7.1	4.1	13.6	6.4	3.5
8	20.4	19.8	19.4	99.3	19.2	8.8	0.4	0.1	18.1	6.3	5.5	3.3	10.7	4.7	3.4
9	20.4	19.8	19.4	99.5	19.7	11.5	0.6	0.1	19.2	7.0	9.1	5.0	15.8	8.1	3.6
10	20.5	19.8	19.5	99.5	19.7	10.9	0.5	0.1	18.9	6.8	9.5	6.0	12.4	5.2	3.5
11	20.5	19.8	19.5	99.5	19.4	9.4	0.3	0.1	18.4	6.4	7.7	5.1	9.3	3.7	3.4
12	20.4	19.8	19.5	99.5	19.8	12.1	0.6	0.1	19.3	7.1	11.6	7.0	14.6	6.8	3.6
13	20.3	19.8	19.4	99.4	19.4	9.8	0.3	0.1	18.7	6.6	9.1	5.4	11.8	4.6	3.5
14	20.3	19.8	19.4	99.3	18.9	8.3	0.2	0.1	18.0	6.2	6.9	4.3	8.5	3.1	3.4
15	20.3	19.8	19.4	99.5	19.6	11.0	0.4	0.1	19.2	7.0	11.4	6.5	13.9	6.2	3.6
16	20.5	19.8	19.3	99.1	19.6	10.6	0.5	0.1	17.9	5.8	8.8	5.3	11.0	4.4	3.5
17	20.5	19.8	19.1	98.7	19.1	9.1	0.3	0.1	17.1	5.5	7.0	4.4	8.1	3.2	3.4
18	20.5	19.8	19.3	99.1	19.7	11.8	0.6	0.2	18.5	6.2	10.9	6.3	13.4	5.9	3.6
19	20.3	19.8	19.4	99.7	19.6	10.0	0.3	0.1	19.3	7.5	10.1	6.1	12.7	5.4	3.5
20	20.3	19.8	19.4	99.6	19.3	8.5	0.2	0.1	18.8	7.1	7.8	5.0	9.7	3.8	3.4
21	20.3	19.8	19.4	99.8	19.7	11.2	0.3	0.1	19.7	7.9	12.3	7.3	14.6	7.1	3.6
S.2 BS	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.4	19.8	19.5	99.4	19.7	10.6	0.4	0.1	19.3	7.0	9.3	5.8	12.2	4.9	3.5
2	20.4	19.8	19.5	99.5	19.3	9.1	0.3	0.1	18.8	6.7	7.6	4.9	9.2	3.6	3.4
3	20.3	19.8	19.5	99.5	19.8	11.8	0.5	0.1	19.7	7.4	11.8	7.0	14.6	6.8	3.6
4	20.4	19.8	19.4	99.4	19.7	10.7	0.4	0.1	19.4	7.2	12.0	7.9	10.3	3.7	3.5
5	20.4	19.8	19.4	99.3	19.4	9.2	0.3	0.1	18.9	6.8	9.7	6.7	7.0	2.5	3.4
6	20.3	19.8	19.4	99.4	19.8	11.9	0.5	0.1	19.7	7.5	14.1	9.2	12.6	5.2	3.6
7	20.4	19.8	19.4	99.4	19.7	10.6	0.5	0.1	19.3	7.1	7.4	4.3	13.9	6.7	3.5
8	20.4	19.8	19.4	99.4	19.4	9.1	0.4	0.1	18.7	6.7	5.8	3.5	11.0	5.0	3.4
9	20.3	19.8	19.4	99.4	19.8	11.8	0.6	0.2	19.7	7.4	9.4	5.2	16.0	8.4	3.6
10	20.4	19.8	19.5	99.5	19.8	11.2	0.5	0.1	19.4	7.2	9.9	6.2	12.8	5.4	3.5
11	20.5	19.8	19.5	99.5	19.5	9.7	0.4	0.1	18.9	6.8	8.0	5.3	9.6	3.9	3.4
12	20.4	19.8	19.4	99.5	19.9	12.3	0.6	0.2	19.8	7.5	12.0	7.3	14.9	7.1	3.6
13	20.3	19.8	19.4	99.4	19.6	10.1	0.3	0.1	19.2	7.0	9.5	5.7	12.2	4.8	3.5
14	20.3	19.8	19.4	99.4	19.2	8.5	0.3	0.1	18.6	6.6	7.3	4.6	8.8	3.3	3.4
15	20.3	19.8	19.4	99.4	19.7	11.3	0.4	0.1	19.7	7.4	11.8	6.9	14.3	6.5	3.6
16	20.5	19.8	19.2	98.9	19.7	10.9	0.6	0.1	18.5	6.2	9.2	5.6	11.4	4.7	3.5
17	20.5	19.8	19.1	98.6	19.3	9.4	0.4	0.1	17.7	5.9	7.3	4.7	8.4	3.3	3.4
18	20.5	19.8	19.2	98.9	19.8	12.1	0.6	0.2	19.0	6.6	11.3	6.6	13.7	6.2	3.6
19	20.3	19.8	19.4	99.7	19.7	10.3	0.3	0.1	19.8	8.0	10.5	6.4	13.0	5.7	3.5
20	20.3	19.8	19.4	99.7	19.4	8.7	0.3	0.1	19.3	7.6	8.2	5.3	9.9	4.0	3.4
21	20.2	19.8	19.4	99.7	19.8	11.4	0.4	0.1	20.1	8.3	12.7	7.6	14.9	7.4	3.6

S.2 RobA	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.5	19.9	19.3	99.6	19.9	10.6	0.3	0.1	19.7	7.0	9.4	5.8	12.4	5.2	3.4
2	20.6	19.9	19.4	99.5	19.6	9.0	0.2	0.1	19.1	6.6	7.6	4.9	9.4	3.8	3.3
3	20.5	19.9	19.3	99.5	19.9	11.8	0.4	0.1	20.1	7.4	11.8	7.0	14.6	7.1	3.4
4	20.5	19.9	19.2	99.1	19.9	10.7	0.3	0.1	19.8	7.1	12.1	7.9	10.5	4.0	3.4
5	20.6	19.9	19.2	99.1	19.6	9.1	0.3	0.1	19.2	6.7	9.8	6.6	7.3	2.7	3.3
6	20.5	19.9	19.1	99.1	19.9	11.9	0.4	0.1	20.2	7.5	14.1	9.2	12.6	5.5	3.4
7	20.5	19.9	19.2	99.1	20.0	10.6	0.4	0.1	19.6	7.0	7.5	4.3	14.3	7.0	3.4
8	20.6	19.9	19.2	99.1	19.6	9.0	0.2	0.1	18.9	6.6	5.7	3.5	11.3	5.2	3.3
9	20.5	19.9	19.1	99.0	20.0	11.8	0.5	0.1	20.0	7.4	9.4	5.3	16.1	8.8	3.4
10	20.6	19.9	19.3	99.6	20.0	11.2	0.4	0.1	19.8	7.1	9.8	6.1	12.9	5.7	3.4
11	20.7	19.9	19.4	99.5	19.7	9.5	0.3	0.1	19.2	6.8	7.9	5.2	9.8	4.1	3.3
12	20.6	19.9	19.3	99.6	20.0	12.3	0.4	0.1	20.1	7.5	12.0	7.2	14.8	7.4	3.4
13	20.4	19.9	19.3	99.5	19.8	10.1	0.3	0.1	19.7	6.9	9.6	5.7	12.4	5.2	3.3
14	20.5	19.9	19.3	99.4	19.3	8.4	0.2	0.1	18.9	6.5	7.3	4.6	9.1	3.6	3.3
15	20.4	19.9	19.2	99.4	19.9	11.3	0.3	0.1	20.1	7.4	11.8	7.0	14.3	6.8	3.4
16	20.7	19.9	19.2	99.1	19.9	10.9	0.4	0.1	18.9	6.2	9.2	5.6	11.7	5.0	3.4
17	20.7	19.9	19.2	99.0	19.5	9.3	0.3	0.1	18.0	5.8	7.3	4.6	8.7	3.6	3.3
18	20.6	19.9	19.2	99.0	20.0	12.1	0.4	0.1	19.4	6.5	11.4	6.7	13.8	6.6	3.4
19	20.4	19.9	18.9	98.2	19.9	10.3	0.3	0.1	20.1	7.9	10.3	6.3	13.0	5.9	3.3
20	20.5	19.9	19.0	98.6	19.6	8.7	0.2	0.1	19.5	7.5	8.0	5.1	10.0	4.2	3.3
21	20.4	19.9	18.8	97.9	19.9	11.4	0.3	0.1	20.4	8.3	12.5	7.5	14.7	7.6	3.4
S.2 RobB	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	20.4	19.7	19.2	99.4	19.7	10.5	0.3	0.1	19.5	6.9	9.3	5.7	12.3	5.2	3.3
2	20.4	19.8	19.2	99.4	19.4	8.9	0.2	0.1	18.9	6.6	7.5	4.8	9.3	3.8	3.2
3	20.3	19.7	19.1	99.3	19.8	11.7	0.4	0.1	19.9	7.4	11.7	7.0	14.5	7.0	3.4
4	20.4	19.7	19.0	98.8	19.8	10.6	0.3	0.1	19.6	7.1	12.0	7.8	10.5	4.0	3.3
5	20.4	19.8	19.1	98.9	19.5	9.0	0.3	0.1	19.0	6.7	9.7	6.6	7.2	2.7	3.2
6	20.3	19.7	19.0	98.7	19.8	11.8	0.4	0.1	20.0	7.5	14.0	9.1	12.6	5.5	3.4
7	20.4	19.7	19.1	98.8	19.8	10.5	0.4	0.1	19.5	7.0	7.4	4.3	14.2	6.9	3.3
8	20.4	19.8	19.1	98.8	19.4	8.9	0.2	0.1	18.8	6.6	5.7	3.4	11.2	5.2	3.2
9	20.3	19.7	19.0	98.8	19.9	11.7	0.4	0.1	19.9	7.4	9.3	5.2	16.1	8.7	3.4
10	20.5	19.8	19.2	99.4	19.8	11.1	0.4	0.1	19.7	7.1	9.7	6.1	12.9	5.7	3.3
11	20.5	19.8	19.2	99.4	19.6	9.5	0.3	0.1	19.1	6.7	7.8	5.1	9.7	4.1	3.2
12	20.4	19.7	19.1	99.3	19.9	12.2	0.4	0.1	20.0	7.5	11.9	7.1	14.8	7.3	3.4
13	20.3	19.7	19.1	99.3	19.6	10.0	0.3	0.1	19.5	6.9	9.5	5.7	12.3	5.1	3.3
14	20.3	19.7	19.2	99.3	19.2	8.4	0.2	0.1	18.8	6.5	7.2	4.5	9.0	3.5	3.2
15	20.2	19.7	19.1	99.2	19.7	11.2	0.3	0.1	19.9	7.3	11.8	6.9	14.2	6.8	3.4
16	20.5	19.8	19.1	98.9	19.7	10.8	0.4	0.1	18.8	6.1	9.1	5.6	11.6	5.0	3.3
17	20.6	19.8	19.1	98.8	19.3	9.2	0.3	0.1	17.9	5.8	7.2	4.6	8.7	3.6	3.2
18	20.5	19.7	19.1	98.8	19.8	12.0	0.4	0.1	19.3	6.5	11.3	6.6	13.8	6.6	3.4
19	20.3	19.7	18.7	97.6	19.7	10.2	0.3	0.1	19.9	7.9	10.3	6.2	12.9	5.9	3.3
20	20.3	19.7	18.8	98.0	19.4	8.6	0.2	0.1	19.4	7.5	7.9	5.1	9.9	4.2	3.2
21	20.2	19.7	18.6	97.1	19.8	11.3	0.3	0.1	20.3	8.2	12.4	7.5	14.6	7.6	3.4

S.3 RSL	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.68	3.59	0.02	70.5	3.59	2.27	0.07	0.01	1.75	0.19	1.66	0.97	2.09	1.02	0.49
2	3.70	3.59	0.02	70.5	3.60	1.98	0.03	0.01	1.70	0.18	1.33	0.80	1.74	0.84	0.48
3	3.67	3.58	0.02	70.6	3.58	2.47	0.12	0.02	1.81	0.20	2.07	1.22	2.43	1.24	0.51
4	3.68	3.59	0.02	70.5	3.60	2.29	0.07	0.01	1.77	0.19	1.99	1.28	1.83	0.83	0.50
5	3.70	3.59	0.02	70.4	3.61	1.99	0.03	0.01	1.71	0.18	1.64	1.06	1.44	0.66	0.48
6	3.67	3.58	0.02	70.6	3.59	2.48	0.14	0.02	1.85	0.20	2.31	1.50	2.16	1.01	0.51
7	3.68	3.59	0.02	70.5	3.59	2.28	0.06	0.01	1.79	0.19	1.41	0.78	2.35	1.27	0.50
8	3.69	3.59	0.02	70.4	3.58	1.99	0.02	0.01	1.73	0.18	1.06	0.61	2.01	1.05	0.48
9	3.67	3.58	0.02	70.5	3.59	2.47	0.10	0.02	1.85	0.20	1.78	0.98	2.65	1.47	0.51
10	3.68	3.59	0.02	70.6	3.62	2.42	0.09	0.01	1.82	0.19	1.84	1.12	2.25	1.16	0.50
11	3.69	3.59	0.02	70.6	3.63	2.13	0.04	0.01	1.77	0.18	1.45	0.91	1.86	0.95	0.48
12	3.68	3.58	0.02	70.7	3.60	2.60	0.16	0.02	1.87	0.20	2.20	1.34	2.57	1.36	0.51
13	3.68	3.59	0.02	70.3	3.55	2.15	0.05	0.01	1.71	0.18	1.57	0.90	1.98	0.94	0.49
14	3.69	3.59	0.02	70.2	3.53	1.84	0.02	0.00	1.64	0.17	1.21	0.70	1.61	0.74	0.48
15	3.67	3.58	0.02	70.4	3.55	2.34	0.09	0.01	1.76	0.19	1.92	1.11	2.29	1.12	0.50
16	3.69	3.59	0.01	67.8	3.60	2.29	0.08	0.01	1.33	0.13	1.52	0.89	2.03	0.99	0.50
17	3.70	3.59	0.01	67.8	3.60	1.99	0.03	0.01	1.28	0.12	1.20	0.72	1.67	0.81	0.48
18	3.68	3.58	0.01	67.8	3.58	2.48	0.14	0.02	1.37	0.14	1.86	1.08	2.36	1.17	0.51
19	3.68	3.59	0.04	73.0	3.59	2.25	0.04	0.01	2.24	0.26	1.89	1.12	2.18	1.10	0.49
20	3.69	3.59	0.04	73.0	3.59	1.96	0.02	0.01	2.16	0.25	1.47	0.89	1.81	0.89	0.48
21	3.67	3.58	0.04	73.0	3.58	2.44	0.08	0.01	2.30	0.28	2.24	1.37	2.49	1.30	0.50
S.3 2mm	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.69	3.61	0.02	72.7	3.57	2.07	0.03	0.01	1.71	0.19	1.51	0.86	1.89	0.88	0.46
2	3.69	3.61	0.02	72.4	3.54	1.79	0.02	0.00	1.63	0.18	1.20	0.70	1.56	0.72	0.45
3	3.68	3.60	0.03	72.7	3.57	2.27	0.06	0.01	1.79	0.21	1.89	1.08	2.23	1.08	0.47
4	3.68	3.61	0.02	72.6	3.58	2.09	0.04	0.01	1.72	0.20	1.84	1.15	1.63	0.70	0.46
5	3.69	3.61	0.02	72.2	3.57	1.80	0.02	0.00	1.64	0.18	1.52	0.95	1.27	0.55	0.45
6	3.68	3.60	0.03	72.7	3.58	2.28	0.07	0.01	1.81	0.21	2.14	1.35	1.95	0.87	0.47
7	3.69	3.61	0.02	72.6	3.56	2.08	0.03	0.01	1.72	0.19	1.27	0.67	2.17	1.12	0.46
8	3.69	3.61	0.02	72.3	3.53	1.80	0.02	0.01	1.65	0.18	0.94	0.52	1.84	0.92	0.45
9	3.68	3.60	0.03	72.7	3.57	2.27	0.06	0.01	1.81	0.21	1.61	0.86	2.46	1.31	0.47
10	3.69	3.61	0.02	72.8	3.61	2.23	0.05	0.01	1.82	0.20	1.69	0.99	2.05	1.01	0.46
11	3.69	3.61	0.02	72.7	3.60	1.94	0.03	0.01	1.74	0.19	1.33	0.81	1.68	0.83	0.45
12	3.69	3.61	0.03	72.8	3.61	2.41	0.08	0.02	1.89	0.22	2.03	1.20	2.37	1.19	0.47
13	3.68	3.61	0.02	72.3	3.52	1.94	0.03	0.01	1.63	0.19	1.43	0.79	1.78	0.80	0.46
14	3.69	3.61	0.02	71.9	3.47	1.65	0.01	0.00	1.53	0.17	1.09	0.61	1.43	0.63	0.45
15	3.67	3.60	0.03	72.4	3.52	2.14	0.05	0.01	1.71	0.20	1.75	0.98	2.09	0.98	0.47
16	3.69	3.61	0.02	69.6	3.57	2.09	0.04	0.01	1.31	0.14	1.38	0.78	1.82	0.85	0.46
17	3.70	3.61	0.01	69.5	3.53	1.80	0.02	0.01	1.25	0.13	1.09	0.63	1.47	0.69	0.45
18	3.69	3.60	0.02	69.8	3.58	2.28	0.07	0.01	1.38	0.14	1.70	0.95	2.13	1.02	0.48
19	3.68	3.61	0.04	73.2	3.57	2.05	0.03	0.01	2.17	0.27	1.72	0.98	1.98	0.95	0.46
20	3.69	3.61	0.04	73.0	3.55	1.77	0.02	0.00	2.06	0.26	1.34	0.77	1.63	0.76	0.45
21	3.68	3.60	0.04	73.3	3.57	2.24	0.06	0.01	2.26	0.29	2.05	1.21	2.29	1.14	0.47

S.3 BS	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.67	3.59	0.03	73.1	3.58	2.15	0.04	0.01	2.11	0.26	1.55	0.87	2.02	0.94	0.47
2	3.69	3.59	0.03	73.1	3.55	1.86	0.02	0.01	2.02	0.24	1.22	0.71	1.66	0.77	0.45
3	3.67	3.59	0.03	73.2	3.60	2.35	0.06	0.01	2.20	0.28	1.94	1.11	2.38	1.17	0.48
4	3.67	3.59	0.03	73.1	3.58	2.16	0.04	0.01	2.12	0.26	1.87	1.17	1.76	0.76	0.47
5	3.69	3.59	0.03	73.0	3.57	1.87	0.02	0.01	2.01	0.24	1.54	0.96	1.36	0.58	0.45
6	3.67	3.59	0.03	73.1	3.60	2.36	0.09	0.01	2.22	0.28	2.17	1.38	2.11	0.94	0.48
7	3.67	3.59	0.03	73.0	3.58	2.16	0.04	0.01	2.13	0.26	1.31	0.69	2.29	1.20	0.47
8	3.69	3.59	0.03	72.9	3.55	1.86	0.02	0.01	2.03	0.25	0.96	0.52	1.94	0.98	0.45
9	3.67	3.58	0.03	73.0	3.60	2.36	0.06	0.01	2.23	0.28	1.66	0.88	2.61	1.40	0.48
10	3.68	3.59	0.03	73.2	3.61	2.30	0.05	0.01	2.20	0.27	1.72	1.01	2.19	1.08	0.47
11	3.69	3.59	0.03	73.2	3.60	2.01	0.03	0.01	2.11	0.25	1.35	0.81	1.79	0.87	0.45
12	3.67	3.59	0.03	73.2	3.64	2.49	0.09	0.02	2.27	0.29	2.07	1.22	2.52	1.29	0.48
13	3.66	3.59	0.03	72.9	3.54	2.02	0.03	0.01	2.05	0.25	1.46	0.81	1.91	0.87	0.47
14	3.68	3.59	0.03	72.7	3.49	1.72	0.01	0.00	1.93	0.23	1.11	0.62	1.53	0.67	0.45
15	3.66	3.58	0.03	72.9	3.57	2.22	0.05	0.01	2.15	0.27	1.80	1.01	2.24	1.06	0.48
16	3.68	3.59	0.02	70.8	3.56	2.18	0.04	0.01	1.65	0.18	1.41	0.80	1.93	0.91	0.47
17	3.69	3.59	0.02	71.0	3.54	1.87	0.02	0.01	1.57	0.17	1.10	0.63	1.56	0.72	0.45
18	3.67	3.58	0.02	70.7	3.58	2.37	0.09	0.01	1.73	0.20	1.74	0.98	2.27	1.09	0.48
19	3.67	3.59	0.05	75.0	3.57	2.12	0.03	0.01	2.49	0.35	1.75	1.00	2.12	1.02	0.46
20	3.68	3.59	0.05	75.2	3.53	1.83	0.02	0.00	2.40	0.33	1.36	0.78	1.74	0.81	0.45
21	3.66	3.58	0.05	74.7	3.58	2.31	0.06	0.01	2.59	0.37	2.08	1.23	2.45	1.23	0.48
S.3 RobA	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.70	3.61	0.03	73.2	3.56	2.05	0.03	0.01	2.09	0.25	1.37	0.71	1.86	0.82	0.44
2	3.71	3.62	0.03	73.2	3.54	1.75	0.02	0.01	2.00	0.24	1.03	0.55	1.46	0.64	0.43
3	3.69	3.61	0.03	73.3	3.57	2.26	0.05	0.01	2.21	0.27	1.80	0.96	2.34	1.05	0.45
4	3.69	3.61	0.03	73.1	3.58	2.06	0.04	0.01	2.16	0.26	1.72	1.00	1.60	0.65	0.44
5	3.71	3.61	0.03	73.0	3.55	1.76	0.02	0.01	2.05	0.24	1.34	0.79	1.17	0.48	0.43
6	3.69	3.61	0.03	73.0	3.59	2.27	0.06	0.01	2.29	0.28	2.06	1.22	2.07	0.84	0.45
7	3.70	3.61	0.03	73.1	3.58	2.06	0.03	0.01	2.15	0.26	1.15	0.56	2.17	1.06	0.45
8	3.71	3.62	0.03	73.0	3.54	1.76	0.02	0.01	2.04	0.24	0.78	0.39	1.76	0.84	0.43
9	3.69	3.61	0.03	73.1	3.59	2.26	0.05	0.01	2.24	0.27	1.53	0.76	2.54	1.28	0.46
10	3.71	3.61	0.03	73.3	3.59	2.20	0.05	0.01	2.22	0.27	1.54	0.83	2.03	0.94	0.45
11	3.72	3.62	0.03	73.3	3.59	1.91	0.03	0.01	2.13	0.25	1.14	0.64	1.58	0.74	0.43
12	3.70	3.61	0.03	73.2	3.60	2.40	0.07	0.01	2.32	0.28	1.92	1.06	2.49	1.15	0.46
13	3.69	3.61	0.03	73.0	3.51	1.92	0.02	0.01	2.01	0.25	1.31	0.67	1.77	0.76	0.44
14	3.70	3.61	0.03	72.9	3.48	1.61	0.01	0.00	1.89	0.23	0.92	0.48	1.34	0.56	0.43
15	3.68	3.60	0.03	73.0	3.53	2.13	0.04	0.01	2.13	0.26	1.68	0.88	2.15	0.96	0.45
16	3.71	3.61	0.02	71.7	3.57	2.08	0.04	0.01	1.71	0.18	1.23	0.64	1.76	0.78	0.45
17	3.73	3.62	0.02	71.8	3.53	1.77	0.02	0.01	1.61	0.17	0.90	0.48	1.35	0.60	0.43
18	3.71	3.61	0.02	71.4	3.58	2.28	0.06	0.01	1.81	0.20	1.59	0.83	2.15	0.97	0.46
19	3.69	3.61	0.04	74.9	3.55	2.02	0.03	0.01	2.58	0.35	1.60	0.84	2.03	0.89	0.44
20	3.70	3.61	0.04	74.9	3.54	1.73	0.02	0.00	2.48	0.33	1.16	0.62	1.54	0.68	0.43
21	3.68	3.60	0.04	74.5	3.58	2.22	0.05	0.01	2.69	0.37	1.97	1.10	2.44	1.12	0.45

S.3 RobB	CTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	3.70	3.61	0.03	73.2	3.56	2.05	0.03	0.01	2.09	0.25	1.37	0.71	1.86	0.82	0.44
2	3.71	3.62	0.03	73.2	3.54	1.75	0.02	0.01	2.00	0.24	1.03	0.55	1.46	0.64	0.43
3	3.69	3.61	0.03	73.3	3.57	2.26	0.05	0.01	2.21	0.27	1.80	0.96	2.34	1.05	0.45
4	3.69	3.61	0.03	73.1	3.58	2.06	0.04	0.01	2.16	0.26	1.72	1.00	1.60	0.65	0.44
5	3.71	3.61	0.03	73.0	3.55	1.76	0.02	0.01	2.05	0.24	1.34	0.79	1.17	0.48	0.43
6	3.69	3.61	0.03	73.0	3.59	2.27	0.06	0.01	2.29	0.28	2.06	1.22	2.07	0.84	0.45
7	3.70	3.61	0.03	73.1	3.58	2.06	0.03	0.01	2.15	0.26	1.15	0.56	2.17	1.06	0.45
8	3.71	3.62	0.03	73.0	3.54	1.76	0.02	0.01	2.04	0.24	0.78	0.39	1.76	0.84	0.43
9	3.69	3.61	0.03	73.1	3.59	2.26	0.05	0.01	2.24	0.27	1.53	0.76	2.54	1.28	0.46
10	3.71	3.61	0.03	73.3	3.59	2.20	0.05	0.01	2.22	0.27	1.54	0.83	2.03	0.94	0.45
11	3.72	3.62	0.03	73.3	3.59	1.91	0.03	0.01	2.13	0.25	1.14	0.64	1.58	0.74	0.43
12	3.70	3.61	0.03	73.2	3.60	2.40	0.07	0.01	2.32	0.28	1.92	1.06	2.49	1.15	0.46
13	3.69	3.61	0.03	73.0	3.51	1.92	0.02	0.01	2.01	0.25	1.31	0.67	1.77	0.76	0.44
14	3.70	3.61	0.03	72.9	3.48	1.61	0.01	0.00	1.89	0.23	0.92	0.48	1.34	0.56	0.43
15	3.68	3.60	0.03	73.0	3.53	2.13	0.04	0.01	2.13	0.26	1.68	0.88	2.15	0.96	0.45
16	3.71	3.61	0.02	71.7	3.57	2.08	0.04	0.01	1.71	0.18	1.23	0.64	1.76	0.78	0.45
17	3.73	3.62	0.02	71.8	3.53	1.77	0.02	0.01	1.61	0.17	0.90	0.48	1.35	0.60	0.43
18	3.71	3.61	0.02	71.4	3.58	2.28	0.06	0.01	1.81	0.20	1.59	0.83	2.15	0.97	0.46
19	3.69	3.61	0.04	74.9	3.55	2.02	0.03	0.01	2.58	0.35	1.60	0.84	2.03	0.89	0.44
20	3.70	3.61	0.04	74.9	3.54	1.73	0.02	0.00	2.48	0.33	1.16	0.62	1.54	0.68	0.43
21	3.68	3.60	0.04	74.5	3.58	2.22	0.05	0.01	2.69	0.37	1.97	1.10	2.44	1.12	0.45
S.4 RSL	GTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.52	5.43	5.21	98.4	3.65	0.62	0.00	0.00	2.00	0.22	0.18	0.08	0.15	0.05	0.25
2	5.53	5.43	5.15	98.2	3.12	0.52	0.00	0.00	1.79	0.19	0.14	0.06	0.13	0.05	0.24
3	5.50	5.42	5.27	98.5	4.25	0.74	0.00	0.00	2.26	0.25	0.21	0.11	0.19	0.05	0.26
4	5.52	5.43	5.20	98.4	3.78	0.65	0.00	0.00	2.07	0.23	0.24	0.11	0.10	0.04	0.25
5	5.53	5.43	5.17	98.1	3.12	0.54	0.00	0.00	1.86	0.20	0.18	0.08	0.10	0.04	0.24
6	5.50	5.42	5.21	98.6	4.19	0.76	0.00	0.00	2.34	0.26	0.28	0.14	0.13	0.04	0.26
7	5.52	5.43	5.24	98.5	3.73	0.62	0.00	0.00	2.03	0.22	0.15	0.07	0.26	0.07	0.25
8	5.53	5.43	5.16	98.2	3.08	0.51	0.00	0.00	1.77	0.19	0.11	0.05	0.20	0.07	0.24
9	5.51	5.42	5.26	98.6	4.27	0.73	0.00	0.00	2.26	0.25	0.17	0.10	0.32	0.09	0.26
10	5.53	5.42	5.27	99.2	3.97	0.73	0.00	0.00	2.25	0.25	0.20	0.10	0.19	0.07	0.25
11	5.54	5.43	5.23	99.0	3.45	0.61	0.00	0.00	2.03	0.22	0.17	0.08	0.18	0.07	0.24
12	5.53	5.42	5.29	99.3	4.49	0.83	0.00	0.00	2.50	0.28	0.23	0.12	0.23	0.07	0.26
13	5.51	5.42	5.15	98.0	3.41	0.54	0.00	0.00	1.83	0.20	0.16	0.08	0.12	0.04	0.25
14	5.54	5.43	5.08	97.1	2.78	0.44	0.00	0.00	1.59	0.17	0.12	0.05	0.10	0.03	0.24
15	5.49	5.42	5.19	98.2	3.95	0.65	0.00	0.00	2.05	0.23	0.19	0.10	0.17	0.04	0.26
16	5.55	5.42	4.81	92.8	3.55	0.62	0.00	0.00	1.43	0.14	0.17	0.08	0.16	0.06	0.25
17	5.54	5.43	4.68	91.9	2.91	0.52	0.00	0.00	1.26	0.12	0.13	0.06	0.15	0.06	0.24
18	5.55	5.42	4.86	93.0	4.07	0.72	0.00	0.00	1.63	0.16	0.20	0.11	0.19	0.06	0.26
19	5.52	5.44	5.12	96.6	3.81	0.63	0.00	0.00	2.68	0.33	0.18	0.08	0.15	0.04	0.25
20	5.52	5.44	5.15	99.3	3.30	0.52	0.00	0.00	2.38	0.29	0.13	0.06	0.11	0.04	0.24
21	5.51	5.43	5.11	91.3	4.19	0.74	0.00	0.00	2.92	0.37	0.21	0.11	0.20	0.05	0.26

S.4 2mm	GTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.49	5.42	5.12	98.0	3.57	0.61	0.00	0.00	1.92	0.21	0.15	0.07	0.14	0.05	0.25
2	5.51	5.42	5.10	97.9	3.03	0.50	0.00	0.00	1.70	0.18	0.12	0.06	0.13	0.05	0.24
3	5.49	5.41	5.21	98.2	4.18	0.72	0.00	0.00	2.15	0.24	0.17	0.09	0.18	0.05	0.26
4	5.50	5.41	5.12	97.9	3.69	0.64	0.00	0.00	1.99	0.22	0.20	0.09	0.10	0.03	0.25
5	5.51	5.42	5.11	97.9	3.05	0.52	0.00	0.00	1.79	0.19	0.15	0.07	0.09	0.03	0.24
6	5.48	5.40	5.13	98.1	4.12	0.74	0.00	0.00	2.26	0.25	0.23	0.12	0.12	0.04	0.26
7	5.51	5.41	5.16	98.2	3.68	0.61	0.00	0.00	1.90	0.21	0.12	0.06	0.24	0.07	0.25
8	5.51	5.42	5.09	97.9	2.99	0.50	0.00	0.00	1.64	0.18	0.09	0.04	0.19	0.06	0.24
9	5.49	5.41	5.17	98.3	4.15	0.71	0.00	0.00	2.17	0.24	0.14	0.08	0.30	0.08	0.26
10	5.52	5.42	5.21	98.3	3.92	0.71	0.00	0.00	2.17	0.24	0.17	0.09	0.18	0.06	0.25
11	5.52	5.42	5.14	98.0	3.36	0.60	0.00	0.00	1.94	0.21	0.15	0.07	0.17	0.06	0.24
12	5.51	5.41	5.23	98.5	4.42	0.82	0.00	0.00	2.39	0.27	0.19	0.10	0.22	0.07	0.26
13	5.49	5.41	5.07	97.9	3.34	0.53	0.00	0.00	1.74	0.19	0.13	0.07	0.11	0.03	0.25
14	5.51	5.41	5.01	95.9	2.72	0.42	0.00	0.00	1.51	0.16	0.10	0.05	0.09	0.03	0.24
15	5.47	5.40	5.11	97.9	3.89	0.63	0.00	0.00	1.94	0.22	0.16	0.09	0.15	0.04	0.26
16	5.52	5.39	4.71	92.4	3.47	0.61	0.00	0.00	1.36	0.14	0.15	0.07	0.15	0.05	0.25
17	5.50	5.39	4.63	91.1	2.83	0.50	0.00	0.00	1.19	0.12	0.12	0.05	0.15	0.05	0.24
18	5.52	5.39	4.80	92.3	4.01	0.71	0.00	0.00	1.57	0.16	0.17	0.09	0.17	0.06	0.26
19	5.50	5.42	5.30	99.8	3.71	0.62	0.00	0.00	2.57	0.32	0.15	0.07	0.14	0.04	0.25
20	5.51	5.43	5.27	99.7	3.24	0.51	0.00	0.00	2.28	0.28	0.12	0.05	0.11	0.04	0.24
21	5.48	5.40	5.29	99.9	4.10	0.72	0.00	0.00	2.79	0.36	0.17	0.09	0.19	0.05	0.26
S.4 BS	GTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.55	5.42	5.31	100.0	3.70	0.61	0.00	0.00	2.40	0.29	0.14	0.07	0.14	0.05	0.25
2	5.58	5.43	5.30	99.9	3.09	0.51	0.00	0.00	2.15	0.26	0.12	0.05	0.12	0.04	0.24
3	5.53	5.41	5.30	100.0	4.24	0.73	0.00	0.00	2.70	0.33	0.17	0.09	0.18	0.05	0.26
4	5.55	5.42	5.31	99.9	3.75	0.64	0.00	0.00	2.58	0.30	0.20	0.09	0.09	0.03	0.25
5	5.57	5.43	5.30	99.8	3.17	0.52	0.00	0.00	2.29	0.27	0.15	0.07	0.09	0.03	0.24
6	5.54	5.41	5.29	99.9	4.17	0.75	0.00	0.00	2.81	0.34	0.23	0.11	0.12	0.04	0.26
7	5.55	5.42	5.29	100.0	3.71	0.61	0.00	0.00	2.40	0.29	0.12	0.06	0.24	0.07	0.25
8	5.57	5.42	5.29	99.9	3.09	0.50	0.00	0.00	2.10	0.25	0.09	0.04	0.18	0.06	0.24
9	5.54	5.41	5.28	100.0	4.21	0.72	0.00	0.00	2.73	0.33	0.14	0.07	0.30	0.08	0.26
10	5.57	5.42	5.30	100.0	4.05	0.72	0.00	0.00	2.75	0.33	0.17	0.08	0.18	0.06	0.25
11	5.58	5.42	5.30	99.9	3.45	0.60	0.00	0.00	2.43	0.29	0.15	0.07	0.17	0.06	0.24
12	5.55	5.42	5.28	100.0	4.48	0.82	0.00	0.00	3.01	0.37	0.19	0.10	0.22	0.07	0.26
13	5.55	5.41	5.30	99.9	3.43	0.54	0.00	0.00	2.18	0.26	0.13	0.06	0.11	0.03	0.25
14	5.55	5.42	5.30	99.7	2.75	0.43	0.00	0.00	1.87	0.23	0.10	0.04	0.09	0.03	0.24
15	5.54	5.40	5.29	100.0	3.95	0.64	0.00	0.00	2.43	0.30	0.15	0.08	0.15	0.04	0.26
16	5.54	5.42	5.22	99.7	3.61	0.61	0.00	0.00	1.86	0.20	0.15	0.07	0.15	0.05	0.25
17	5.53	5.42	5.17	98.6	2.95	0.50	0.00	0.00	1.60	0.17	0.12	0.05	0.14	0.05	0.24
18	5.55	5.42	5.27	99.8	4.05	0.72	0.00	0.00	2.10	0.22	0.17	0.09	0.17	0.05	0.26
19	5.53	5.41	5.06	91.0	3.88	0.62	0.00	0.00	3.12	0.43	0.14	0.07	0.14	0.04	0.25
20	5.55	5.41	5.09	93.2	3.44	0.51	0.00	0.00	2.83	0.38	0.11	0.05	0.10	0.04	0.24
21	5.52	5.39	5.04	90.6	4.28	0.73	0.00	0.00	3.37	0.48	0.17	0.09	0.19	0.05	0.26

S.4 RobA	GTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.48	5.41	5.31	99.8	3.93	0.64	0.00	0.00	2.41	0.28	0.17	0.08	0.14	0.04	0.26
2	5.51	5.41	5.32	99.8	3.28	0.53	0.00	0.00	2.18	0.25	0.13	0.06	0.11	0.04	0.25
3	5.47	5.40	5.29	99.9	4.34	0.77	0.00	0.00	2.72	0.31	0.21	0.11	0.19	0.05	0.26
4	5.47	5.40	5.27	99.6	3.95	0.68	0.00	0.00	2.46	0.29	0.24	0.10	0.09	0.03	0.26
5	5.50	5.41	5.27	99.6	3.34	0.54	0.00	0.00	2.22	0.25	0.17	0.07	0.07	0.03	0.25
6	5.47	5.39	5.26	99.6	4.38	0.79	0.00	0.00	2.78	0.32	0.29	0.14	0.12	0.03	0.26
7	5.49	5.40	5.28	99.8	3.97	0.65	0.00	0.00	2.46	0.28	0.14	0.07	0.25	0.07	0.26
8	5.53	5.41	5.29	99.9	3.29	0.52	0.00	0.00	2.16	0.24	0.10	0.05	0.18	0.05	0.25
9	5.47	5.39	5.27	99.9	4.35	0.77	0.00	0.00	2.72	0.31	0.17	0.09	0.32	0.09	0.26
10	5.50	5.41	5.32	100.0	4.26	0.74	0.00	0.00	2.70	0.31	0.20	0.09	0.17	0.05	0.26
11	5.55	5.41	5.32	100.0	3.62	0.61	0.00	0.00	2.42	0.28	0.16	0.07	0.14	0.05	0.25
12	5.48	5.40	5.31	100.0	4.58	0.87	0.00	0.00	2.95	0.34	0.23	0.12	0.22	0.06	0.26
13	5.47	5.40	5.22	99.6	3.66	0.58	0.00	0.00	2.22	0.26	0.15	0.07	0.12	0.03	0.26
14	5.49	5.40	5.22	99.4	2.97	0.45	0.00	0.00	1.96	0.22	0.11	0.05	0.08	0.03	0.25
15	5.46	5.39	5.20	98.9	4.06	0.69	0.00	0.00	2.48	0.29	0.19	0.10	0.17	0.04	0.26
16	5.51	5.40	5.09	97.8	3.93	0.65	0.00	0.00	1.80	0.19	0.16	0.08	0.14	0.04	0.26
17	5.55	5.40	5.11	97.3	3.23	0.52	0.00	0.00	1.58	0.16	0.12	0.05	0.11	0.04	0.25
18	5.50	5.39	5.08	97.8	4.41	0.76	0.00	0.00	2.01	0.21	0.20	0.10	0.18	0.05	0.26
19	5.48	5.40	5.22	99.8	3.96	0.66	0.00	0.00	3.14	0.41	0.17	0.08	0.15	0.04	0.26
20	5.48	5.40	5.23	99.5	3.57	0.53	0.00	0.00	2.88	0.37	0.13	0.05	0.10	0.03	0.25
21	5.48	5.39	5.21	99.7	4.34	0.77	0.00	0.00	3.39	0.45	0.21	0.11	0.21	0.05	0.26
S.4 RobB	GTV				Br.		Ch.		SC		L. Co.		R. Co.		Ext.
Scn.	$D_{2\%}$	$D_{50\%}$	$D_{98\%}$	$V_{95\%}$	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	$D_{2\%}$	Mean	Mean
1	5.48	5.41	5.28	99.6	3.96	0.65	0.00	0.00	2.36	0.27	0.15	0.07	0.09	0.03	0.25
2	5.51	5.41	5.29	99.6	3.30	0.53	0.00	0.00	2.13	0.24	0.12	0.05	0.07	0.03	0.24
3	5.47	5.40	5.28	99.8	4.41	0.78	0.00	0.00	2.66	0.31	0.19	0.10	0.11	0.03	0.26
4	5.47	5.40	5.23	99.2	4.01	0.68	0.00	0.00	2.42	0.28	0.22	0.10	0.06	0.02	0.25
5	5.49	5.40	5.24	99.2	3.43	0.55	0.00	0.00	2.18	0.25	0.16	0.07	0.05	0.02	0.24
6	5.46	5.40	5.21	98.9	4.40	0.80	0.00	0.00	2.74	0.31	0.26	0.13	0.07	0.02	0.26
7	5.50	5.41	5.27	99.9	4.04	0.65	0.00	0.00	2.43	0.27	0.12	0.06	0.15	0.05	0.25
8	5.53	5.41	5.29	99.8	3.29	0.52	0.00	0.00	2.13	0.24	0.09	0.04	0.12	0.04	0.24
9	5.48	5.40	5.27	99.9	4.39	0.77	0.00	0.00	2.69	0.31	0.15	0.08	0.18	0.05	0.26
10	5.50	5.41	5.32	99.9	4.28	0.75	0.00	0.00	2.67	0.30	0.18	0.09	0.11	0.04	0.25
11	5.54	5.42	5.31	99.9	3.63	0.61	0.00	0.00	2.38	0.27	0.15	0.07	0.10	0.03	0.24
12	5.48	5.41	5.31	99.9	4.64	0.87	0.00	0.00	2.93	0.34	0.21	0.11	0.13	0.04	0.26
13	5.47	5.40	5.18	99.2	3.69	0.58	0.00	0.00	2.18	0.25	0.14	0.07	0.07	0.02	0.25
14	5.49	5.40	5.19	98.9	2.97	0.45	0.00	0.00	1.92	0.22	0.10	0.05	0.06	0.02	0.24
15	5.46	5.39	5.19	99.0	4.11	0.70	0.00	0.00	2.43	0.28	0.17	0.09	0.09	0.03	0.26
16	5.51	5.41	5.09	97.7	3.98	0.65	0.00	0.00	1.77	0.18	0.15	0.07	0.10	0.03	0.25
17	5.54	5.41	5.09	96.8	3.28	0.52	0.00	0.00	1.55	0.16	0.12	0.05	0.08	0.03	0.24
18	5.50	5.40	5.07	97.6	4.44	0.77	0.00	0.00	1.98	0.21	0.18	0.09	0.11	0.04	0.26
19	5.47	5.40	5.22	99.4	4.01	0.66	0.00	0.00	3.10	0.40	0.16	0.08	0.09	0.03	0.25
20	5.48	5.40	5.23	99.2	3.51	0.53	0.00	0.00	2.84	0.36	0.12	0.05	0.07	0.02	0.24
21	5.47	5.39	5.21	99.3	4.37	0.78	0.00	0.00	3.35	0.45	0.19	0.10	0.10	0.03	0.26