DOSIMETRIC COMPARISON OF RAPIDPLAN AND MANUALLY OPTIMIZED PLANS FOR HIPPOCAMPUS AVOIDANCE WHOLE BRAIN RADIATION THERAPY

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A Thesis Submitted in Partial Fulfillment of the Requirements
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การเปรียบเทียบปริมาณรังสีระหว่างการวางแผนการรักษาแบบอัตโนมัติโดยใช้โปรแกรม RapidPlan และวางแผนแบบแมนนวลในการฉายรังสีสมองแบบป้องกันสมองส่วนฮิปโปแคมปัส

น.ส.ลักษมณ พิมลอัศวคุณ

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ลักษมณ พิมลอัศวคุณ : การเปรียบเทียบปริมาณรังสีระหว่างการวางแผนการรักษาแบบอัตโนมัติโดยใช้โปรแกรม RapidPlan และวางแผนแบบแมนนวลในการฉายรังสีสมองแบบป้องกันสมองส่วนฮิปโปแคมปัส. (DOSIMETRIC COMPARISON OF RAPIDPLAN AND MANUALLY OPTIMIZED PLANS FOR HIPPOCAMPUS AVOIDANCE WHOLE BRAIN RADIATION THERAPY) อ.ที่ปรึกษาหลัก : ผศ. ดร.ทวีป แสงแห่งธรรม, อ.ที่ปรึกษาร่วม : อ. ดร.อิศรา อิศรางกูร ณ อยุธยา

ปัจจุบันการฉายรังสีแบบครอบคลุมทั้งสมอง (WBRT) เป็นวิธีที่นิยมในการรักษามะเร็งระยะแพร่กระจายสู่สมอง (brain metastases) แต่อย่างไรก็ตามก็มีการรายงานว่าการฉายรังสีแบบครอบคลุมทั้งสมองสามารถส่งผลเสียต่อสมองส่วนฮิปโปแคมปัสได้ ซึ่งสมองส่วนนี้มีบทบาทสำคัญในการสร้างความทรงจำระยะยาว ดังนั้นจึงมีการคิดค้นวิธีที่ฉายรังสีครอบคลุมทั้งสมองและป้องกันสมองส่วนฮิปโปแคมปัสไปด้วยกัน (HA-WBRT) ซึ่งวิธีการฉายแบบนี้สามารถใช้ร่วมกับเทคนิคการฉายแบบปรับความเข้ม intensity-modulated radiotherapy (IMRT) และ volumetric-modulated arc therapy (VMAT) ได้อีกด้วย โดยการฉายรังสีแบบ HA-WBRT เป็นการวางแผนการรักษาที่มีความยากและซับซ้อนขึ้นอยู่กับผู้วางแผนการรักษาเป็นอย่างมาก ทางคณะผู้วิจัยจึงต้องการลดความซับซ้อนในจุดนี้โดยการใช้ knowledge-based planning นั่นก็คือโปรแกรม RapidPlan มาช่วยในการวางแผนการรักษา ดังนั้นจุดประสงค์ของการศึกษานี้คือเพื่อเปรียบเทียบปริมาณรังสีในการวางแผน HA-WBRT แบบ VMAT ระหว่างใช้ RapidPlan และแบบแมนนวล โดยทำการสร้าง RapidPlan model สำหรับ HA-WBRT ขึ้นมา กำหนดปริมาณรังสีที่ PTV และ OARs ตามเกณฑ์ของ RTOG 0933 จำนวนเคสในการสร้างโมเดลอยู่ที่ 20 เคส ส่วนการเปรียบเทียบ RapidPlan และแมนนวลแพลนใช้ทั้งหมด 10 เคส ทุกเคสกำหนด prescribed dose ที่ PTV เท่ากับ 30 Gy ผลการศึกษาพบว่าที่ PTV เทคนิคการ optimize แบบ RapidPlan มีประสิทธิภาพมากกว่าแบบแมนนวล โดยที่ $D_{90\%}$ เท่ากันของทั้ง RapidPlan และ manual plans มีค่า $D_{98\%}$ ของ RapidPlan และแมนนวลแพลนอยู่ที่ 27.69±0.98 Gy และ 25.83±1.86 Gy ตามลำดับ ขณะที่ CI และ HI พบว่า RapidPlan สามารถทำได้ดีกว่าแมนนวลแพลน ในส่วนของฮิปโปแคมปัส D_{max} ของ RapidPlan และแมนนวลแพลนอยู่ที่ 15.66±1.29 Gy และ 14.42±1.23 Gy ตามลำดับ ซึ่งปริมาณรังสีของทั้ง 2 แบบไม่ได้แตกต่างกันอย่างมีนัยสำคัญ ($p>0.05$) ค่า $D_{100\%}$ ของ RapidPlan และแมนนวลแพลนอยู่ที่ 9.25±0.35 Gy และ 8.72±0.55 Gy ตามลำดับ ขณะที่จอประสาทตาพบว่า RapidPlan สามารถลดปริมาณรังสีได้ดีกว่าแบบแมนนวลแพลนแต่ในทางกลับกัน แมนนวลแพลนสามารถลดปริมาณรังสีในเลนส์ตาได้ดีกว่า RapidPlan

โดยสรุปการฉายรังสี HA-WBRT ในเทคนิค VMAT โดยใช้ RapidPlan และแมนนวลแพลนสามารถคุมปริมาณรังสีให้อยู่ในเกณฑ์ของ RTOG 0933 ได้ โดย RapidPlan สามารถทำ PTV coverage ได้ดีกว่าแมนนวลแพลนอีกทั้งยังมีความเข้ารูปของเส้นแสดงปริมาณรังสีที่ดีกว่าแมนนวลแพลนอย่างมีนัยสำคัญ และถึงแม้ว่าแมนนวลแพลนทำได้ดีกว่า RapidPlan ในส่วนของฮิปโปแคมปัสแต่ไม่ได้แตกต่างอย่างมีนัยสำคัญ ดังนั้น RapidPlan สามารถนำไปใช้ในทางคลินิกได้และอาจปรับเปลี่ยนการ optimize เล็กน้อยเพื่อให้ได้แพลนที่ดียิ่งขึ้น

สาขาวิชา	ฟิสิกส์การแพทย์	ลายมือชื่อนิสิต .....
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Laksamon Phimolasawakun : DOSIMETRIC COMPARISON OF RAPIDPLAN AND MANUALLY OPTIMIZED PLANS FOR HIPPOCAMPUS AVOIDANCE WHOLE BRAIN RADIATION THERAPY. Advisor: Asst. Prof. TAWEAP SANGHANGTHUM, Ph.D. Co-advisor: Isra Israngkul Na Ayuthaya, Ph.D.

Nowadays, whole-brain radiation therapy (WBRT) is a good method to cure brain metastases. However, it has been noted that whole-brain radiation therapy could be a cause to neurological toxicity which could damage the hippocampus that is an important part of forming long-term memories. The HA-WBRT is a complicated plan depending on planner skills, the researcher would like to simplify this problem using knowledge-based planning called RapidPlan. The objective of this study was to compare the dosimetric difference of RapidPlan and manually optimized plans for the treatment of HA-WBRT. The RapidPlan model was created for HA-WBRT. The PTV and OARs constraints are followed by RTOG 0933 criteria. Twenty cases were used for creating the RapidPlan model and ten cases were used for comparing RapidPlan and manual plans. The treatment prescription to the whole brain PTV was prescribed to 30 Gy. The results showed the PTV optimization using RapidPlan was more effective than manual plans. With the same D90% of PTV between RapidPlan and manual plans, the D98% of RapidPlan and manual plans were 27.69±0.98 Gy and 25.83±1.86 Gy, respectively. Moreover, RapidPlan showed slightly better in CI and HI of PTV than manual plans. The maximum dose to the hippocampus of RapidPlan and manual plans were 15.66±1.29 Gy and 14.42±1.23 Gy, respectively. The doses between the two optimized types were not significantly different ($p>0.05$). The D100% of hippocampus of RapidPlan and manual plans were 9.25±0.35 Gy and 8.72±0.55 Gy, respectively. On the other hand, RapidPlan can spare more optic nerves than manual plans while manual plans can spare more lenses than RapidPlan.

In conclusion, HA-WBRT in VMAT technique using RapidPlan and a manual plan was able to maintain the radiation dose within the RTOG 0933 constraint. RapidPlan shows better PTV coverage and presents significantly conforms the dose to the target than manually optimized plans. Although the manual plans performed better than RapidPlan in the hippocampus, it was not a significant different. It can be concluded that the RapidPlan can be used in clinical terms with a slight adjustment for well-optimized plans.

Field of Study:	Medical Physics	Student's Signature .....
Academic Year:	2021	Advisor's Signature .....
		Co-advisor's Signature .....

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CHAPTER 1

INTRODUCTION

1.1 Background and rationale

Whole Brain Radiation Therapy (WBRT) is a good brain metastasis treatment that could manage both visible and non-visible tumors micrometastases.[1] However, it has been noted that whole-brain radiation therapy could be a cause to neurological toxicity which could damage the hippocampus. [2] Hippocampus is a brain structure embedded deep in the temporal lobe of each cerebral cortex and it is an important part of the limbic system that is responsible for forming long-term memories.[3] The severity of the side effects depends on advance age, poor performance status, and active extracranial disease.[1] Nowadays, WBRT with hippocampus sparing has been initiated to maintain memories in patients with various techniques including Intensity Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), and Helical Tomotherapy (HT).

The manual planning techniques of hippocampal sparing WBRT is a treatment planning that requires abundant experience and skill of the planner. Moreover, it takes longer to plan compared to conventional WBRT due to the complexity of the plan. Nowadays, with the use of advanced technology, automatic planning has been invented to solve these issues. It is an automated radiotherapy planning platform which advantages as follows.

- Simplify and accelerate IMRT/VMAT planning
- Enhance plan consistency and quality
- Simplify and standardize the plan approval process

To create automatic planning, a manual treatment plan is required for the program to learn. Since King Chulalongkorn Memorial Hospital does not yet have automatic planning for hippocampus sparing WBRT, the researchers have realized the importance and benefits of the existence of automatic planning for hippocampus

sparing WBRT. The result of the study will be compared with the manual planning with the use of dosimetric parameters.

For this reason, the researchers realized that the creation of automatic planning for hippocampus sparing WBRT could facilitate the treatment planning and reduce the limitation of the planner's experience. Furthermore, it will reduce the workload and can be applied to clinically at King Chulalongkorn Memorial Hospital.

1.2 Research objective

To compare the dosimetric differences between using a RapidPlan and manually optimized plans for the treatment of HA-WBRT.

CHAPTER 2
REVIEW OF RELATED LITERATURES

2.1 Radiotherapy Techniques

2.1.1 3D Conformal Radiation Therapy (3D-CRT)[4]

3D conformal radiation therapy is a type of cancer treatment in which the radiation beams are shaped to match the tumor's shape using MLC. Previously, radiation beams were simply matched to the tumor's height and width, exposing healthy tissue to the radiation. The precise location of the tumors is now possible to locate with the use of advanced imaging technology. Conformal radiation treatment use targeting information to accurately target the tumor while sparing the healthy tissue in the surrounding area. A number of cancer types have been improved outcomes from 3D-CRT, including Head and neck cancer, Liver cancer, Prostate cancer and Brain cancer.

In treatment planning of 3D-CRT technique, the target localization can be performed using anatomical imaging such as computed tomography, magnetic resonance imaging and ultrasound. When the tumor localization and OARs surrounding has been identified, the number of beams and beam boundaries in patient were designed using beam’s eye view. For whole brain irradiation, this technique is commonly used right and left parallel opposing fields as presented in figure 2.1[5], however, this 3D-CRT plan cannot spare the hippocampus[6].

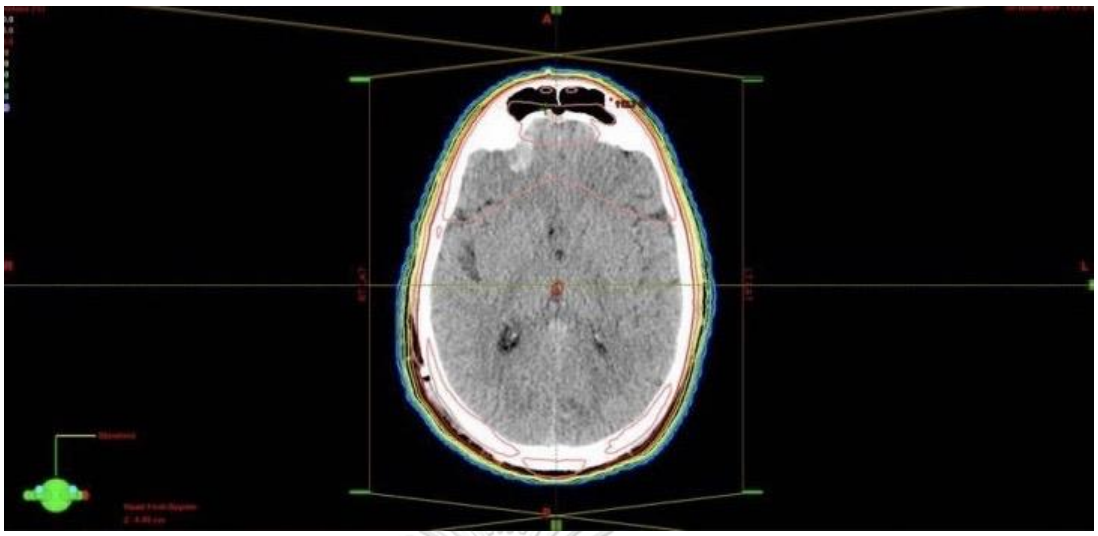


Figure 2.1 Beam on fields of 3D-CRT for WBRT.

2.1.2 Intensity-modulated radiation therapy (IMRT)[7]

Intensity-modulated radiation treatment (IMRT) is a sort of asymmetrical radiotherapy in which a linear accelerator is used to deliver an advanced type of high-precision radiotherapy in which the radiation beam is shaped to precisely suit the tumor's area. A multi-leaf collimator (MLC) is a device on the linear accelerator made up of tiny leaves that move independently and generate forms that fit perfectly around the treatment zone. The intensity of IMRT beams were modulated by MLC movement. The movement of MLC can be divided into 2 types: step and shoot and dynamic MLC.

IMRT uses a non-uniform beam in each beam over multiple beam angles to obtain the desired radiation dose distribution. The intensity was calculated by a computer and called inverse planning. The target dose and OARs dose were determined first then the computer system was reverse calculated to move MLC to different locations using various speeds.

The main advantage of IMRT technique was the isodose distribution that can conform to the shape of tumor volume. At the same time, the OARs received a low dose which represents good dose sparing. In addition, IMRT

can irradiate multiple tumors at the same time. IMRT technique has key parameters such as energy, beam direction and the number of beams then proceed to the optimization process.

IMRT calculations have a good dose distribution. However, the limitation of IMRT technique is the higher of monitor unit (MU) than 3D-CRT technique, which increases the risk of secondary cancer and the problem of long-time irradiation. These problems led to the development of VMAT technique. The example of IMRT beam on fields for whole-brain irradiation is shown in figure 2.2[8].

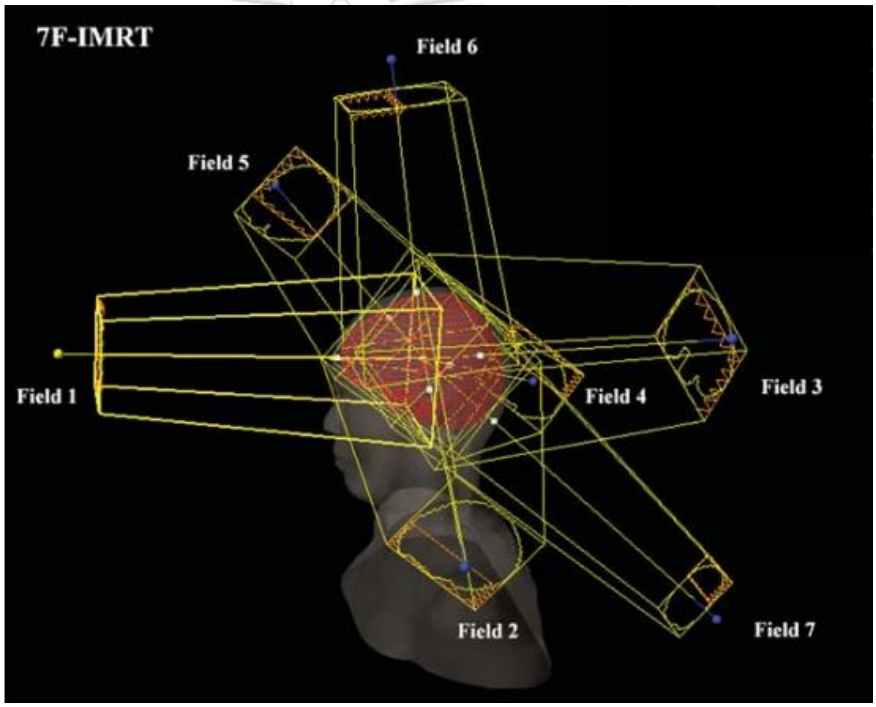


Figure 2.2 Beam on fields of 7F-IMRT plan for WBRT.

2.1.3 Volumetric Modulated Arc Therapy (VMAT)[7]

Volumetric Modulated Arc Therapy (VMAT) is a novel form of IMRT. During irradiation, the linear accelerator circulates around the patient. As it goes, the machine constantly reshapes and adjusts the strength of the radiation beam. The beam intensity can be modulated by MLC movement, dose rate, and gantry speed variation.

This radiotherapy technique ensures high accuracy, reduces treatment time, and utilizes a lower overall dosage of radiation. In the treatment, a linear accelerator (LINAC) must be utilized. Practically, this technique permits applying the treatment considerably more quickly than other techniques with one or more rotation arcs. Treatment with a single arc of 360° can be performed in under 2 minutes. Both VAMT and IMRT are equally effective for normal tissue sparing. However, the treatment time in VMAT is significantly shorter than IMRT.

The intensity modulation of VMAT technique still uses the same inverse planning optimization principles as the IMRT technique, but with a more complex process and takes a longer time optimization than IMRT technique.

The VMAT technique has the advantage of reducing the monitor unit. Thereby reducing irradiation time. However, the use of VMAT produces a wide low dose area because the radiation dose is given around the patient.

The VMAT is shown particularly for the therapy of head and neck tumors with specific qualities, as well as prostate cancer and central nervous system tumors. The example of VMAT beam on fields for whole-brain irradiation is shown in figure 2.3[8].

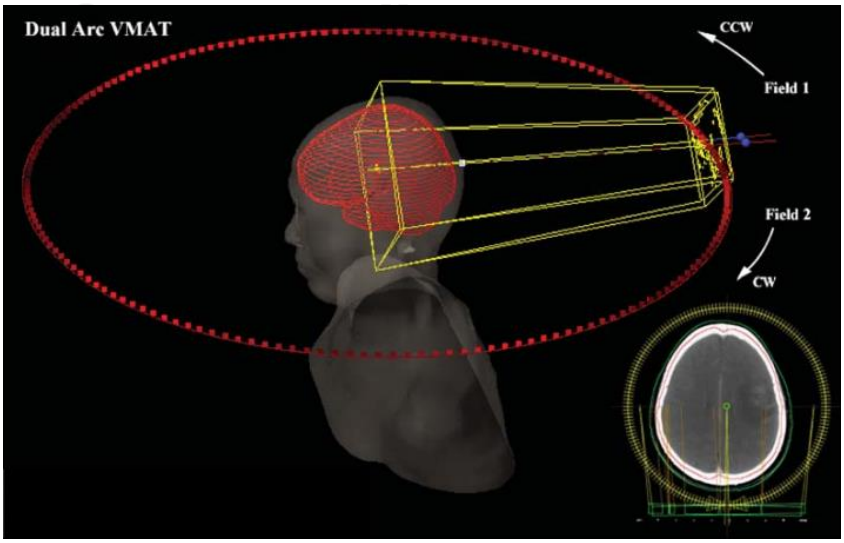


Figure 2.3 Beam on fields of dual arc VMAT for WBRT.

2.2 Whole brain radiation therapy

2.2.1 Overview[9]

Whole-brain radiation therapy (WBRT) is a form of external radiation therapy that is used for treating patients with brain cancer. It is frequently used to treat brain metastases patients or patients with multiple tumors that are not surgically removed. Over many weeks, radiation is delivered to the whole brain. This type of therapy can be mentioned as whole-brain radiation therapy or whole-brain radiotherapy.

2.2.2 Side effect[10]

The utilization of radiation treatment for therapy of brain tumors is restricted by the danger of radiation-induced damage to the normal, healthy brain tissue that can lead to crushing functional deficits. Radiation-induced brain injury is classified as acute, early delayed (subacute), and late delayed reactions based on the timing of beginning symptoms. Acute injury, happening forty-eight hours to a few weeks after WBRT, is fairly mild to moderate in severity and is involved in fatigue, hair loss, skin erythema, headache, nausea, drowsiness, and emesis. Early delayed (subacute) injury is noticed one to six months after WBRT and is related with the clinical symptoms of fatigue, somnolence, short-term cognitive decline, and transient demyelination. Even though acute and early delayed injuries can lead to severe medical conditions, it is regularly believed that most of the signs and symptoms of these injuries are reversible.

On the other hand, late deferred injury, happening a half year after WBRT, is considered irreversible and progressive and is described by demyelination, vascular abnormalities, and ultimate white matter necrosis. Indeed, progressive impairments in learning and memory were seen in 40-50% of brain tumor patients as long-term results of radiation treatment.

2.3 Brain metastases[11]

2.3.1 Overview

Brain metastases occur when disease cells spread from their unique site to the brain. Any cancer can spread to the brain, but the types probably going to cause brain metastases are breast, lung, kidney, colon and melanoma.

Brain metastases may form one tumor or numerous growths in the brain. As the metastatic brain tumors develop, they create pressure on and change surrounding brain tissue function. This causes signs and symptoms, for example, headache, character change, cognitive decline and seizures.

The therapy for patient whose malignant growth has spread to the brain may include surgery, radiation therapy, chemotherapy, immunotherapy or a combination of treatments. Other treatments may be suggested in specific circumstances. Treatment is often focused on reducing pain and symptoms resulting from the disease. The image of brain metastases is shown in figure 2.4.

2.3.2 Symptoms

Signs and symptoms caused by brain metastases can vary based on the area, size and growth rate of the metastatic tumors.

Signs and symptoms of brain metastases include:

- Headache, vomiting or nausea
- Mental changes, like increasing memory problems
- Seizures
- Numbness or weakness on one side of the body

2.3.3 Causes

Brain metastases occur when cancer cells split away from their original area. The cells may travel through the circulatory system or the lymph system and spread (metastasize) to the brain where start to duplicate.

Metastatic cancer that spreads from its original area is known by the name of the primary cancer. For instance, cancer that has spread from the lung to the brain is called metastatic lung cancer, not brain cancer.

2.3.4 Primary cancer types

Any type of malignant can spread to the brain, yet a few kinds of cancer are more likely to cause brain metastases, including:

- Breast cancer
- Lung cancer
- Kidney cancer
- Colon cancer
- Melanoma

Figure 2.4 Brain metastases.

2.4 Hippocampus[12]

The hippocampus is a brain structure located in the inner folds of the bottom center region of the brain, known as the temporal lobe. The hippocampus has been known to humans for almost four centuries. It is one of the most extensively researched areas of the brain.

Human learning and memory are two of its primary tasks. The hippocampus has benefited researchers in their understanding of memory. The anatomy of the hippocampus is shown in figure 2.5[13]

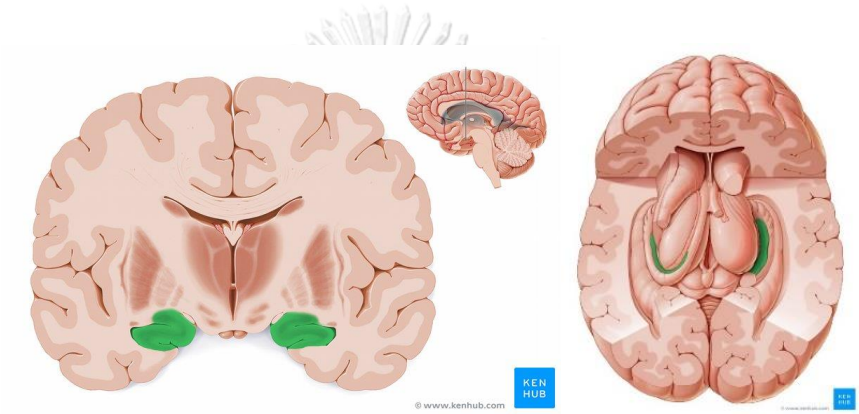


Figure 2.5 Anatomy of hippocampus.

2.5 Knowledge-based planning (RapidPlan)

Knowledge-based planning (KBP) or auto-planning is a volume-driven automatic planning platform in the Eclipse treatment planning system. The traditional KBP methods have been widely investigated in the last decade and have also been clinically implemented. The RapidPlan commercial software is one example of a knowledge-based planning module, which was released in 2014 by Varian Medical Systems. The traditional methods include atlas-based, methods that utilize geometric features and OAR overlap volume histogram either to find the best-matched prior case from a repository or to build dose prediction models.[14]

2.5.1 RapidPlan model construction[15]

The RapidPlan KBP engine comprises of three fundamental subsystems: i) a model training environment, ii) a dose volume histogram

prediction environment, and iii) the generation of personalized dose-volume constraints for the plan optimization.

The first is dedicated to the information displaying of the plan and patient's datasets and the training of the prescient model for each OAR. The second part means to estimate the dose distribution as dose volume histograms, DVH, attainable for a specific new patient, based on the application of the predictive model. The third component gets from the assessed DVH and from a set of customizable rules related to the model. The actual dose-volume constraints to use for the dose optimization.

These constraints could be of different nature: lower, upper, upper gEUD, mean dose, line objectives. This last requirement is a whole DVH, which is used as a single objective: specifically, the line objective is generally used from estimated DVH.

After the model configuration, RapidPlan permits the client to analyze the model quality. the model training is assessed through parameters specific for each structure and each plan in the model configuration. This assessment stage is here considered as a component of the configuration process, where possible outlier plans are identified and managed. On the other side, the model quality is given by a summary of goodness-of-fit and goodness-of-estimation statistics.

2.5.2 RapidPlan optimization[16]

Auto-Planning requires only three simple steps as presented in figure 2.6 to generate a deliverable plan. Only anatomic contours are required to get started.

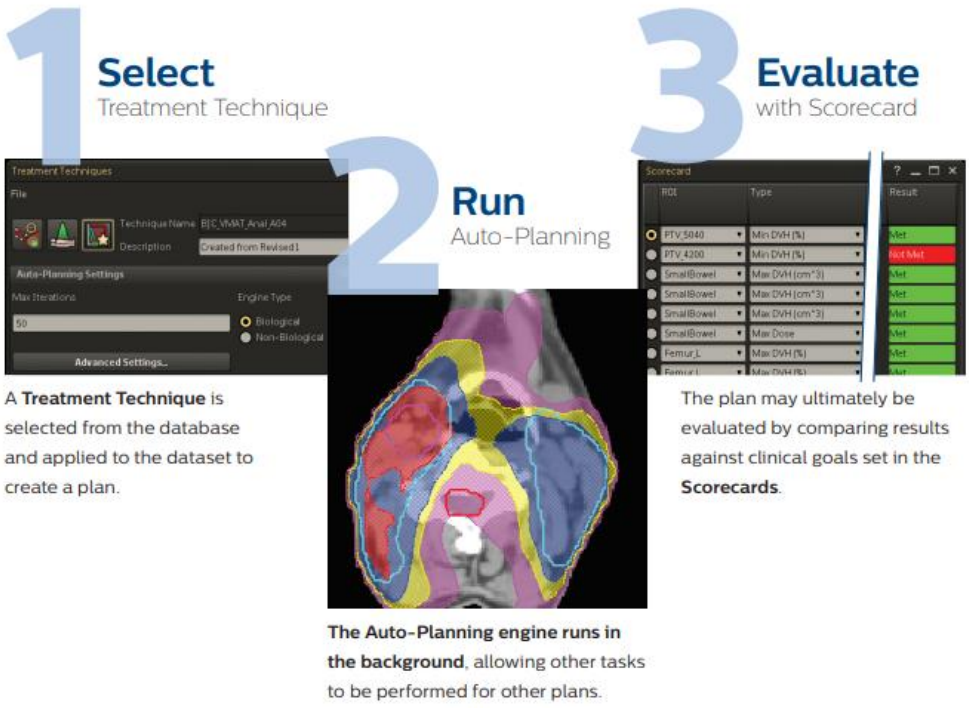


Figure 2.6 Step of Rapid plan optimization.

1) Select a treatment technique

Auto-Planning comes with an example set of treatment procedures, and users may create their library of treatment techniques. They have parameters that are usually manually input or drawn during the IMRT or VMAT planning process. These included the region of interests (ROIs) and point of interests (POIs), isocenter and prescriptions, machine and biological parameters, optimization types, and clinical goals.

2) Run auto planning

It starts the optimization process with the parameters from the specified treatment technique. The operation is run in the background and conducts automated warm starts without the need for operator input. The progress is displayed with a status bar as shown in figure 2.7.

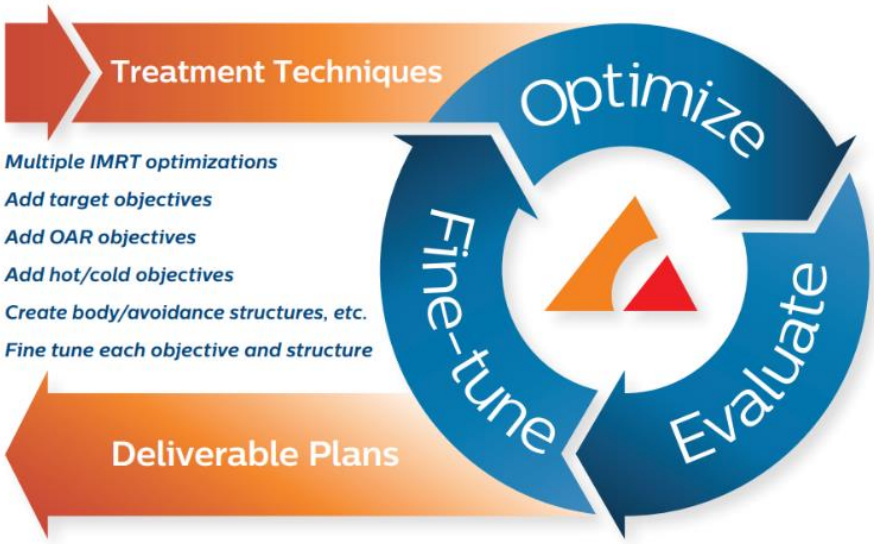


Figure 2.7 Run auto planning cycle.

3) Evaluate with scorecards

Scorecards help to streamline and standardize the time-consuming and inconsistent plan approval process. They provide quick access to information about plan quality that can be compared to clinical objectives. As illustrated in figure 2.8, each scorecard incorporates clinical goals that are commonly used to assess plan quality, including:

• Dose and DVH-based goals for targets and OARs

• Volume comparison goals

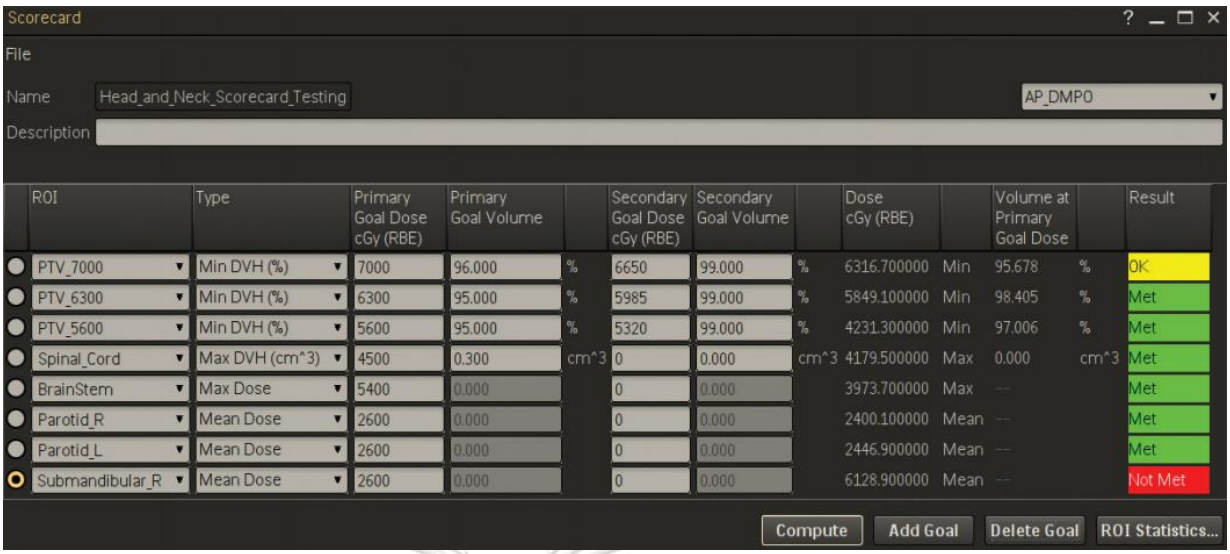


Figure 2.8 Scorecards menu.

2.6 Treatment plan evaluation[17]

After the dose calculations are performed medical physicists on a computer. The radiation oncologists and physicist will evaluate the plan using these following parameters: isodose curves, orthogonal planes/isodose surfaces, dose distribution statistics, and dose volume histograms.

2.6.1 Isodose curves

Isodose curves are lines that join points of equal dose. They offer a planar representation of the dose distribution and effectively show the behavior of one beam or combination of beams with various shielding, wedges, bolus, etc.

Isodose curves are utilized to assess treatment plans along a single plane or over several planes in the patient. The plan is commonly accepted within 95-100% of isodose lines, while the OARs must not exceed the tolerance limits. This approach is ideal if the number of transverse slices is small.

2.6.2 Orthogonal planes and isodose surfaces

When a larger number of transverse planes are utilized for calculation (for example, with a CT scan) it could be unfeasible to evaluate the plan on

the basis of axial slice isodose distributions alone. In such cases, isodose distributions can also be generated on orthogonal CT planes, reproduced from the original axial data. Sagittal and coronal plane isodose distributions are available on most three-dimensional TPSs.

In addition, the radiation dose line can be displayed as a three-dimensional surface. To estimate tumor coverage of a treatment plan, they do not convey a sense of distance between the isosurface and the anatomical volumes and give no quantitative volume information. An example of such a display is shown in figure 2.9.

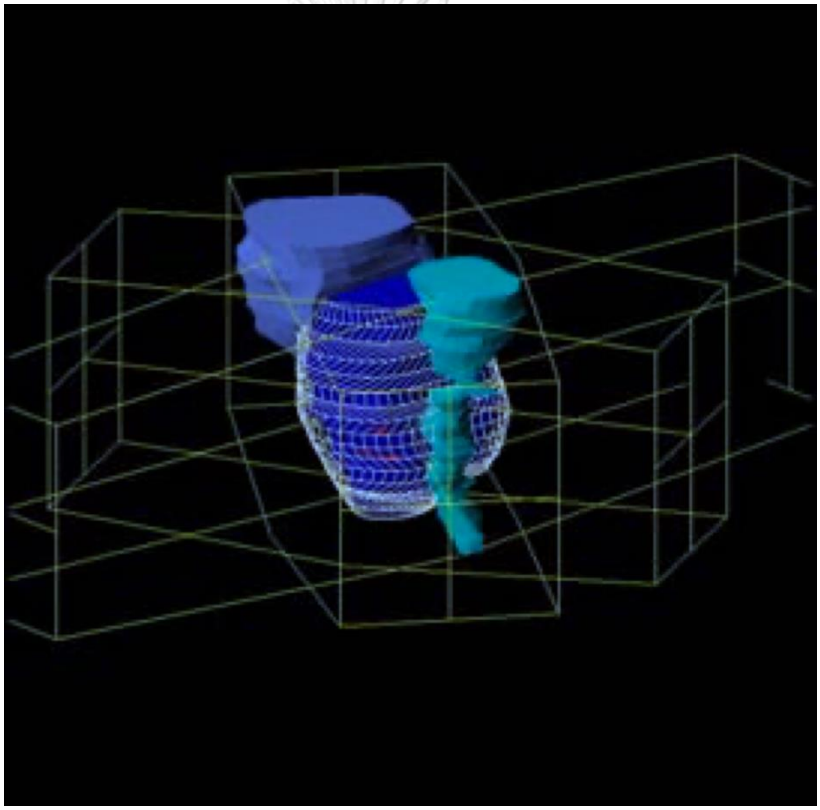


Figure 2.9 A 3-D plot of the prescription isodose (white wireframe) is superimposed on the target volume, with the bladder and the rectum shown.

2.6.3 Dose distribution statistics

The radiation distribution curves do not show a quantitative relationship between tumor volumes or the volume of normal tissue about the received dose. The statistics are simply another method to assess treatment plans. These include:

- The minimum dose to the volume (D_{min});
- The maximum dose to the volume (D_{max});
- The mean dose to the volume (D_{mean});
- The dose received by at least 95% of the volume ($D_{95\%}$);
- The volume irradiated to at least 95% of the prescribed dose ($V_{95\%}$).

2.6.4 Dose-volume histograms

DVHs summarize the data contained in the 3-D dose distribution and are incredibly powerful tools for the quantitative evaluation of treatment plans. Two types of DVH are in use:

- **Direct dose-volume histogram**: To create a direct DVH, the computer sums the number of voxels with an average dose within a given range and plots the resulting volume as a function of dose. The ideal DVH for a target volume would be a single column indicating that 100% of the volume receives the prescribed dose. For a critical structure, the DVH may contain several peaks, indicating that different parts of the organ receive different doses.
- **Cumulative dose-volume histogram**: The cumulative DVH is more popular than the first type. It can display the relationship between the cumulative volume of the tumor. All cumulative DVH plots start at 100% of the volume for 0 Gy, since all of the volume receives at least no dose.

2.7 Parameter indices

2.7.1 Conformity index (CI)[18]

The conformity index is introduced as an extension of section-by-section dosimetric analysis and dose-volume histograms. The conformity index is defined as the ratio of the reference isodose volume (V_{RI}) to the target volume (TV). The conformity index equal to 1 corresponds to the ideal dose coverage or high conformity. Equation 1 demonstrates the empirical

formula to determine the CI. The concept of critical organs is shown in figure 2.10.[19]

$$CI = \frac{V_{RI}}{TV} \qquad (1)$$

where: V_{RI} is the reference isodose volume,

TV is the target volume.

2.7.2 Homogeneity index (HI)[20]

The homogeneity index is used for the homogeneity evaluation of dosage distribution in planning target volume (PTV). The conventional HI is primarily defined as the ratio of the maximum dose (D_{max}) to the minimum dose (D_{min}) or prescription dose in PTV. The HI formula in this study was suggested by ICRU 83. An ideal HI for evaluating radiotherapy plans should objectively and accurately reflect the dose distribution. Equation 2 demonstrates the HI empirical formula selected in this thesis.

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \qquad (2)$$

where: $D_{2\%}$ is the greatest dose delivered to 2% of the PTV,

$D_{98\%}$ is the dose delivered to 98% of the PTV,

$D_{50\%}$ is the dose delivered to 50% of the PTV.

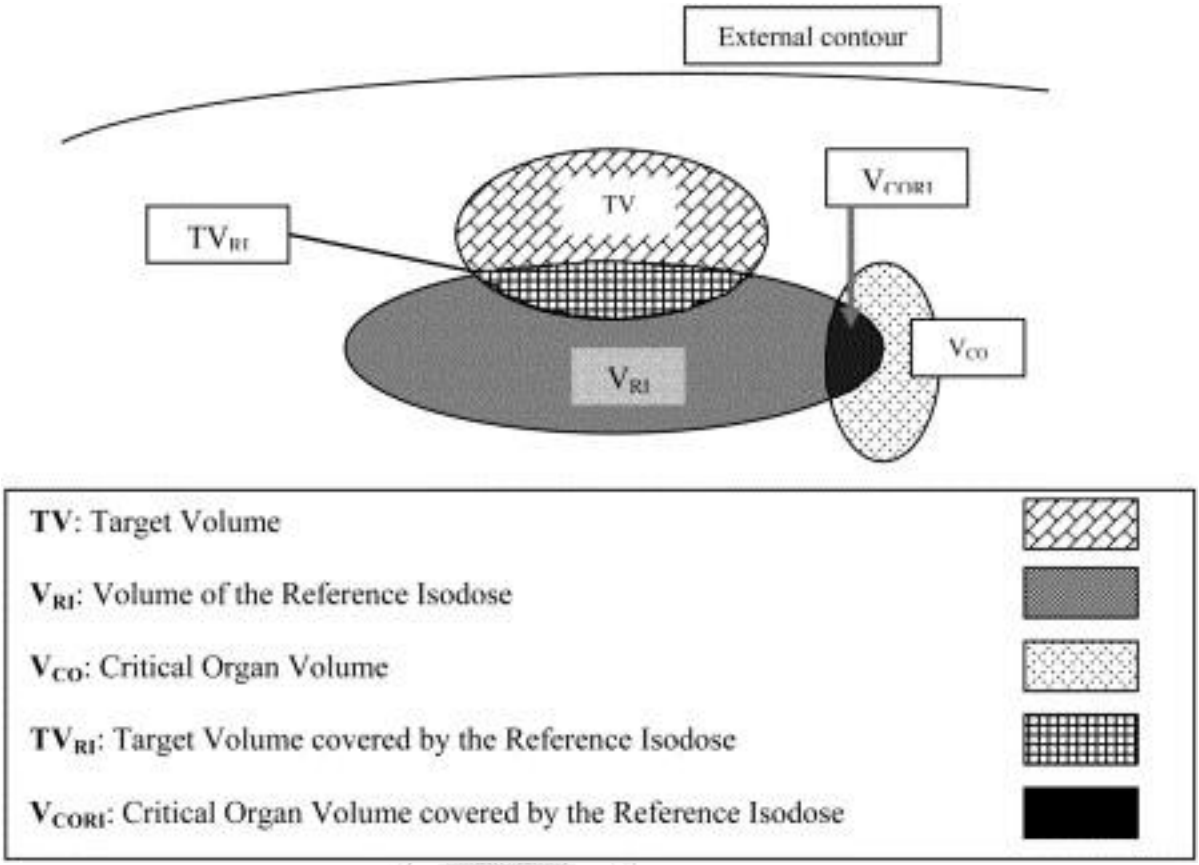


Figure 2.10 Diagram of the various volumes required to calculate the conformity index.

2.8 Review of related literatures

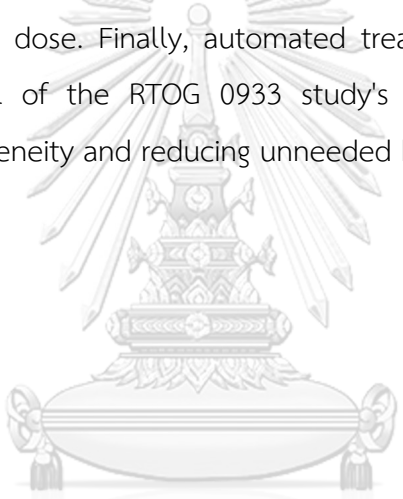
The first literature review, F.Oskan et al. [1] studied in a Hippocampus sparing in whole-brain radiotherapy. The goal of this study was to provide an overview of WBRT neurotoxicity, as well as the technological solutions to these concerns, the distribution of cerebral metastases inside the brain, and the available clinical data. This review research consisted of six publications. Firstly, Blomstrand et al. carried out planning research with four different techniques: standard opposing fields, IMRT, Intensity Modulated Arc Therapy (IMAT), and Intensity Modulated Proton Therapy (IMPT). The results showed CTV coverage was least affected for IMPT plans, suggesting that OARs can be spared to a greater extent with proton technique. Of the highly conformal photon techniques, IMRT was slightly more effective than IMAT at sparing NSC. Another study from Tarnawski et al. showed the possibility of lowering

irradiation dosage to NSC regions while keeping the doses assigned to the PTV using IMRT, Helical Tomotherapy, and VMAT in 10 lung cancer patients. The results showed both helical tomotherapy and LINAC-based IMRT reduced radiation dose to NSC regions by approximately 45%, while maintaining the full dose to the rest of the brain. The next study from Gondi et al. investigated the use of tomotherapy and IMRT to lower the mean dose of the hippocampus. The results showed target coverage and homogeneity were acceptable with both IMRT modalities. Gutierrez and colleagues treated cerebral metastases using a simultaneous integrated boost (SIB) and reported the mean dosage to the hippocampus. The results showed composite tomotherapy plans achieved three objectives: homogeneous whole-brain dose distribution equivalent to conventional WBRT; conformal hippocampal avoidance and radiosurgery-equivalent dose distributions to individual metastases. Hsu et al. conducted similar planning research that used VMAT with equal dosage recommendations and incorporated a SIB approach. The results showed VMAT was able to achieve adequate whole brain coverage with conformal hippocampal avoidance and radiosurgery-quality dose distribution for 1-3 brain metastases. Finally, Prokic and colleagues compared sequential integrated boost (SC) and SIB concepts and discovered that the SIB approach spared the hippocampus more effectively. The results showed both SIB and SC were able to achieve adequate whole brain coverage. SIB achieved better sparing of the hippocampus. In conclusion, NSC sparing with helical tomotherapy and proton treatment was similar to that with LINAC-based IMRT, according to all article data. The modest difference might be partly explained by the machine structure.

The second literature review, Shuo Wang et al.[21]completed automatic planning on hippocampus avoidance whole-brain radiotherapy. The goal of this study was to see how well Auto-Planning performed when it came to HA-WBRT treatment planning. For this retrospective study, ten patients were chosen. Pinnacle Auto-Planning created two types of plans: one using two coplanar volumetric modulated arc therapy (VMAT) and the other using noncoplanar 9F-IMRT. Their findings revealed that auto VMAT and auto 9F-IMRT had similar dosimetric results. As a result, they found that auto 9F-IMRT plans produced more consistent quality plans,

while auto VMAT plans can save treatment time and potential operating mistakes. Finally, the findings suggest that Auto-Planning might be a useful tool for improving the HA-WBRT.

The third literature review, J. Krayenbuehl et al.[22] compared the RTOG 0933 trial to enhanced plan quality with automated radiation planning for the whole brain with hippocampus sparing. The purpose of this study was to see if it was possible to lower the high dosage to normal while still meeting all of the RTOG 0933 dose constraints utilizing an automated treatment planning system (aTPS) planer-independent plan quality. The results revealed a considerable reduction of 4 Gy in the maximum dosage to 2% of the brain, as well as a significant reduction in the minimum hippocampal dose. Finally, automated treatment planning for HS WBRT was able to meet all of the RTOG 0933 study's recommendations while also enhancing dose homogeneity and reducing unneeded hot spots in the normal brain.



CHAPTER 3
RESEARCH METHODOLOGY

3.1 Research Design

This research is an observational research analytic design in the type of retrospective study.

3.2 Research design model

The diagram of research design model is shown in figure 3.1.

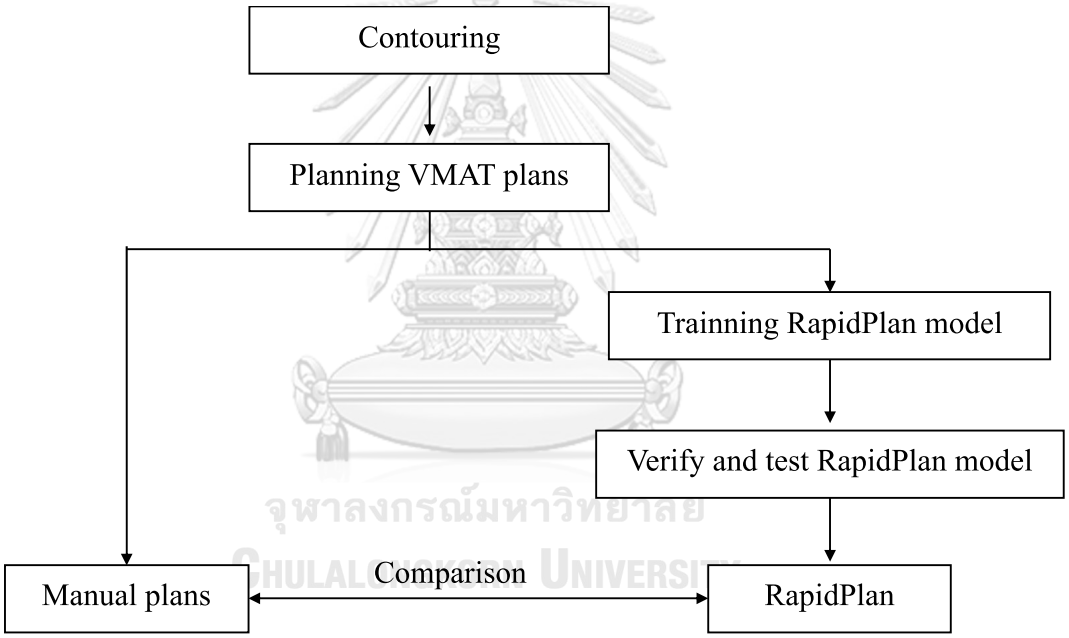


Figure 3.1 Research design model.

3.3 conceptual framework

The factors that affect dosimetric outcomes are planning techniques, optimized techniques, and the experience of planners. The diagram of the conceptual framework is shown in figure 3.2.

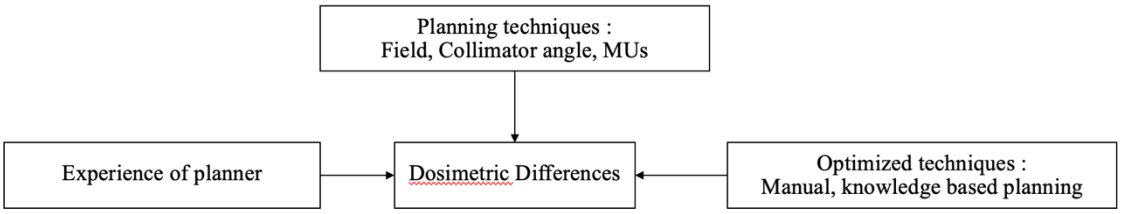


Figure 3.2 Conceptual frameworks.

3.4 Keywords

- Hippocampal avoidance whole-brain radiation therapy (HA-WBRT)
- Volumetric modulated arc therapy (VMAT)
- *Manually optimized plans*
- *RapidPlan*
- *Knowledge-based planning*

3.5 Research question

What are the dosimetric differences between RapidPlan and manually optimized plans for hippocampal avoidance whole brain radiation therapy?

3.6 Materials

The materials used in this study are from the Division of Radiation Oncology, Department of Radiology, King Chulalongkorn Memorial Hospital (KCMH).

1) Eclipse treatment planning system (version 15.6)[23]

Eclipse treatment planning system (version 15.6) (Varian Medical System, Inc, Palo Alto, CA, USA) was used in this study. The Eclipse system improves planning efficiency on multiple levels. Eclipse is designed based on the clinical workflow as shown in figure 3.3. Through every guided step from contouring anatomy to optimizing the plan, to plan approval and peer review,

the workflow is simple, coherent, and streamlined. Integration with the ARIA oncology information system enables the smooth and secure hand-off of the approved plan to the delivery system. Eclipse data becomes easily accessible in ARIA to support further care decision.

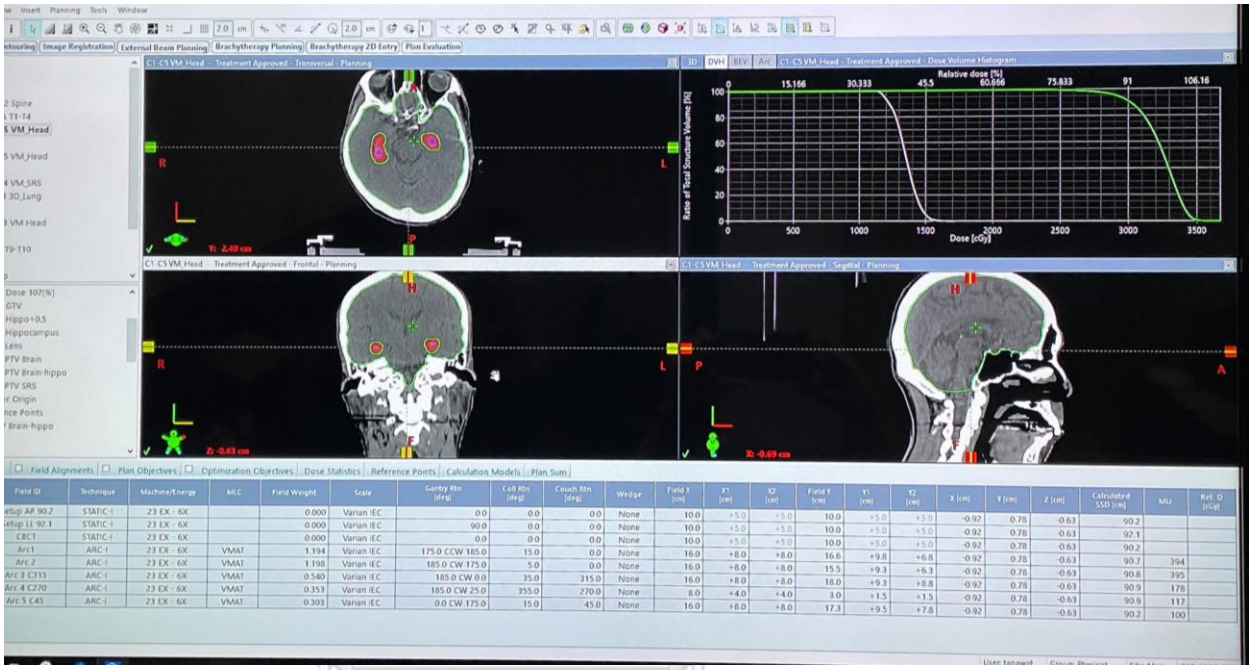


Figure 3.3 Eclipse treatment planning system.

2) RapidPlan[24]

RapidPlan which is knowledge-based planning in Eclipse. RapidPlan raises the standard of quality using models derived from previous high-quality plans as the starting point for new plans. Beginning with a RapidPlan model saves time and improves consistency among planners. In addition, RapidPlan knowledge-based planning establishes a learning system, aided by machine learning, that continuously improves plan quality. The window of RapidPlan model is shown in figure 3.4[15].

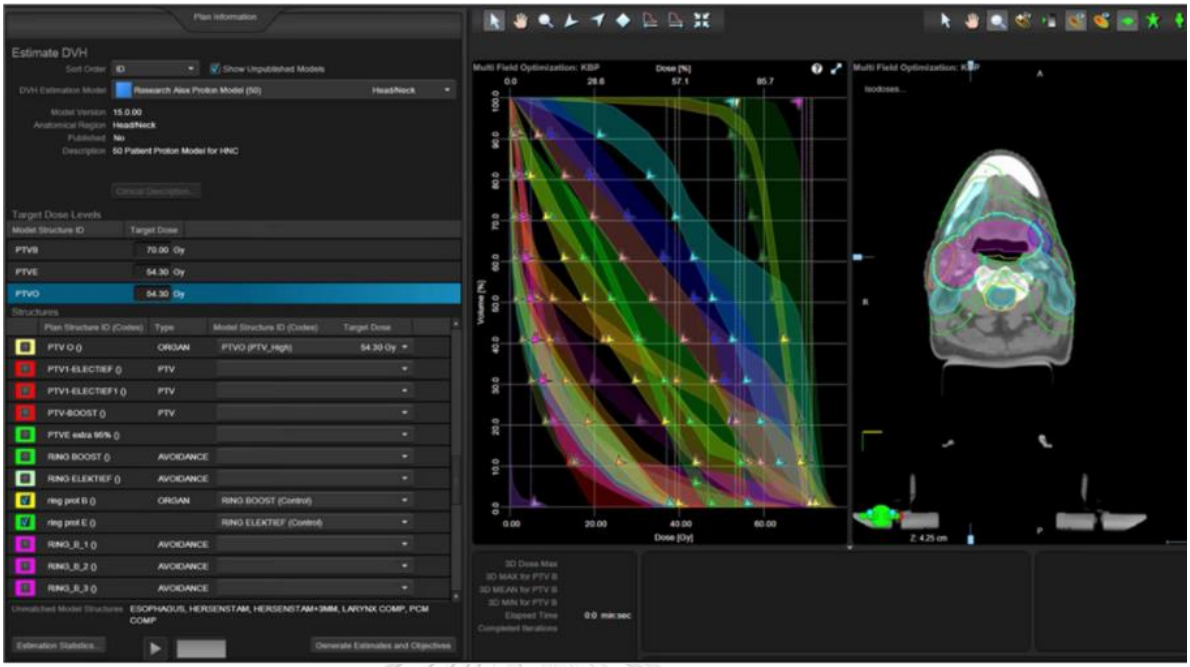


Figure 3.4 RapidPlan model window.

3.7 Methods

This study retrospectively selected the data of brain metastases receiving radiation therapy at the division of radiation oncology, King Chulalongkorn Memorial Hospital. All the imaging data were collected from the ARIA information system and using random sample selection. This research was studied from 30 cases of VMAT technique (20 cases for creating the model and 10 cases for testing) with the inclusion criteria that WBRT patients with brain metastases underwent T1-weighted MRI and CT imaging.

1) Patient selection

The WBRT with hippocampal avoidance cases were collected from the ARIA information system, however, the WBRT alone which has T1-weighted MRI was also added due to the lack of HA-WBRT cases. The sample size is 30 cases and the criteria following by inclusion/exclusion criteria. All selected cases have been irradiated before June 2021.

2) Structure contouring

CT and MRI imaging data were transferred to Eclipse treatment planning version 15.6 (Varian Medical System, Palo Alto, CA, USA) and the brain MRI image was registered with original CT data. The delineations of organs such as PTV, hippocampus, optic nerves, and lens were performed. The PTV represented the brain volume except for the hippocampus and a 0.5 cm margin around the hippocampus. The PTV was separated into upper/middle/lower PTV according to the hippocampus level. The structure contouring is shown in Figure 3.5. The hippocampus was delineated following RTOG 0933 guidelines and manually drawn on a T1-weighted MRI image or 3D contrast-enhanced T1-weighted MRI image. All contours were assessed and approved by the experienced radiation oncologist.

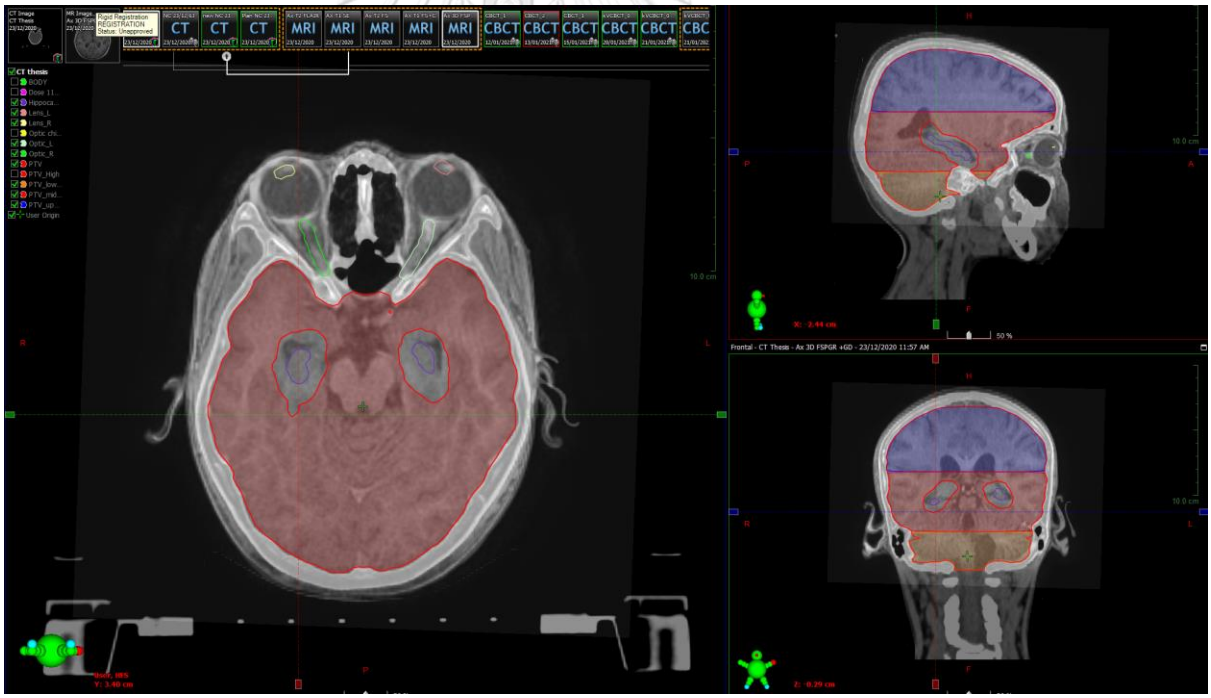


Figure 3.5 The example of structure contouring.

The general principles for hippocampus contouring in this study are including:

- Do not contour the entire hippocampus, but focus mostly on subgranular zone (SGZ)

- Contour the hippocampus on T1-weighted MRI axial sequences.
- Give the preponderance of grey matter in the hippocampus, focus contouring on the T1-hypointense signal medial to the temporal horn.
- Contour from lower slice to upper slice.

The hippocampus contouring is shown in Figure 3.6.[25]

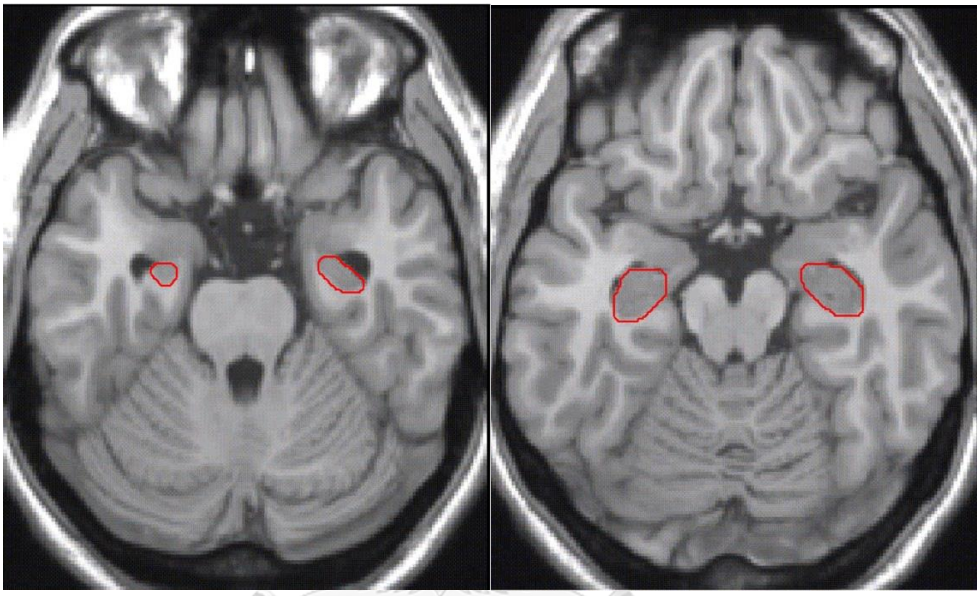


Figure 3.6 The example of hippocampus contouring on T1 weighted MRI.

3) Training RapidPlan model

Delineation results were transferred to Eclipse treatment planning for developing VMAT plans. The 6 MV photon beams were used for dose calculation for all plans. The treatment prescription for the whole brain PTV was prescribed to 30 Gy for 10 fractions. A total of 20 treatment plans were produced in the present study. The whole-brain PTV of all plans was covered by 90% of the prescribed dose. The 20 cases of HA-WBRT plan with VMAT technique will be added to RapidPlan for training. After that set the optimization for RapidPlan and prioritize each organ as shown in figure 3.7. (The RapidPlan optimization window is shown in figure A1.)

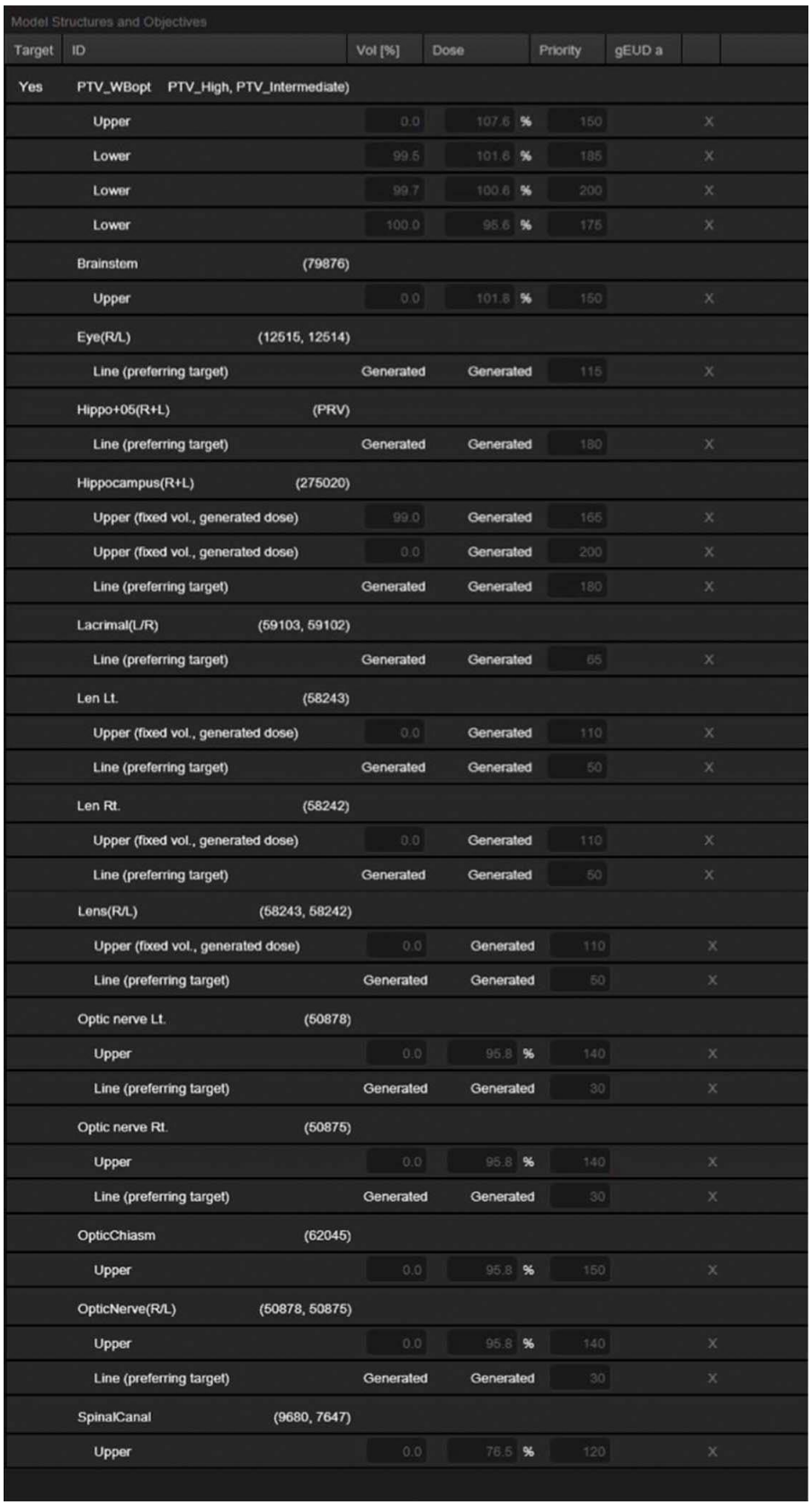


Figure 3.7 Model structure and Objectives for HA-WBRT.

4) Verifying and testing RapidPlan

The accepted auto plans were verified by comparing with previously training plans as shown in the diagram in Figure 3.8. All auto plans were verified under the professional planner who has experienced more than 5 years and then test with other plans which never been learned.

Ten cases were selected for testing plans including 5 new cases and 5 repeating cases which were trained in RapidPlan model. The repeated cases were selected due to the limitation of HA-WBRT cases in the ARIA information system.

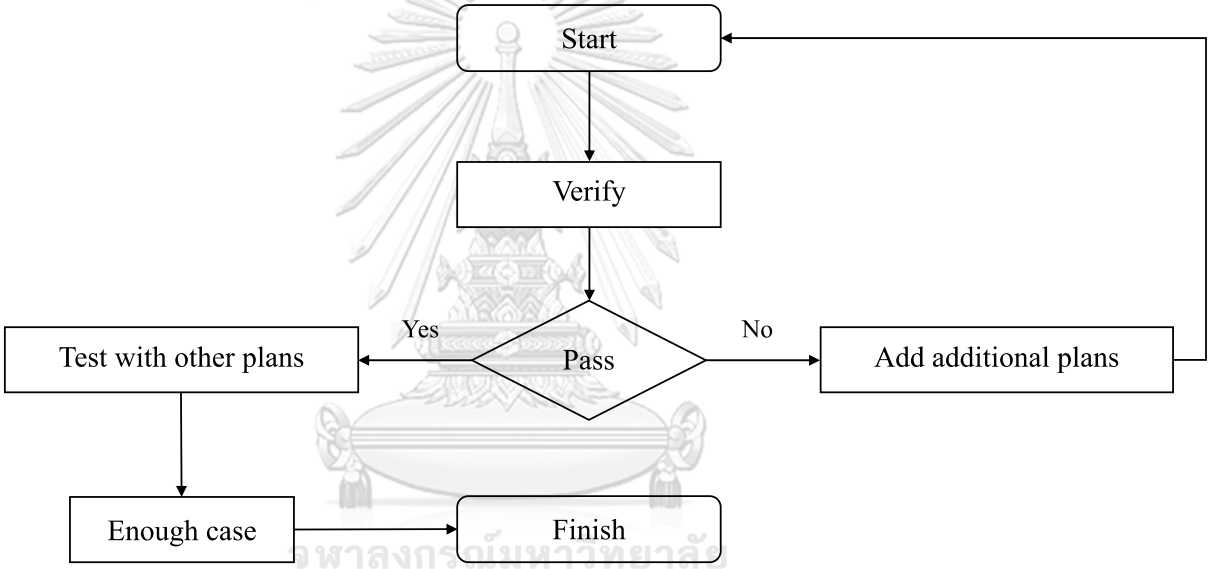


Figure 3.8 Verify and test diagram.

5) Plan evaluation

To evaluate the PTV coverage, the PTV volume should receive a dose of $D_{90\%}$ at least 30 Gy. The hot spot was defined as the dose received by the hottest of 2% of the PTV. Dose-volume histograms (DVH) were calculated for the PTVs and OARs of each plan. Compliance criteria and critical structure constraints in RTOG 0933 as shown in Table 3.1[26] were used to evaluate the plans. The PTV was evaluated using the conformity index (CI_{RTOG}), homogeneity index (HI), $D_{98\%}$ and $D_{2\%}$.

The CI and HI were calculated using equation [1] and [2], respectively.

$$CI = \frac{V_{RI}}{TV} \quad [1]$$

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad [2]$$

where: V_{RI} is the reference isodose volume,

TV is the target volume,

$D_{2\%}$ is the greatest dose delivered to 2% of the PTV,

$D_{98\%}$ is the dose delivered to 98% of the PTV.

$D_{50\%}$ is the dose delivered to 50% of the PTV.

The hippocampus was evaluated using $D_{100\%}$, minimum dose (D_{min}) and mean dose (D_{mean}). The maximum dose (D_{max}) and/or mean dose (D_{mean}) were used to evaluate the other OAR doses.

Table 3.1 Compliance criteria and critical structure constraints in RTOG 0933.

Treatment Component	Parameter	Per Protocol	Variation Acceptable	Deviation Acceptable
MRI/CT Fusion and Contouring	MRI-CT fusion	No corrections to MRI/CT fusion requested	No corrections to MRI/CT fusion requested	Corrections to MRI/CT fusion requested
	Hippocampal Contouring	$\leq$ 2 mm deviation using the Hausdorff distance	> 2, $\leq$ 7 mm deviation using the Hausdorff distance	> 7 mm deviation using the Hausdorff distance
HA-WBRT IMRT/VMAT planning	PTV	D2% $\leq$ 37.5 Gy D98% $\geq$ 25Gy	D2% > 37.5 Gy, $\leq$ 40 Gy D98% < 25Gy	V30 $\leq$ 90% D2% > 40 Gy
	Hippocampus	D100% $\leq$ 9 Gy Maximum dose $\leq$ 16 Gy	D100% $\leq$ 10 Gy Maximum dose $\leq$ 17 Gy	D100% > 10 Gy Maximum dose > 17 Gy
	Optic Nerves and Chiasm	Maximum dose $\leq$ 37.5 Gy	Maximum dose $\leq$ 37.5 Gy	Maximum dose > 37.5 Gy

3.8 Outcome measurements

The outcomes for plan evaluation are:

- Dosimetric parameters of planning target volume (PTV)
- Dosimetric parameters of organs at risk (OARs)
- Homogeneity index (HI)

- Conformity index (CI)
- Dose-volume histogram (DVH)

3.9 Statistical analysis

The paired t-test was performed to test comparisons between RapidPlan and manually plans. A 2-tailed with P-value of lesser than 0.05 was considered statistically significant and all analyses were performed using Microsoft excel.

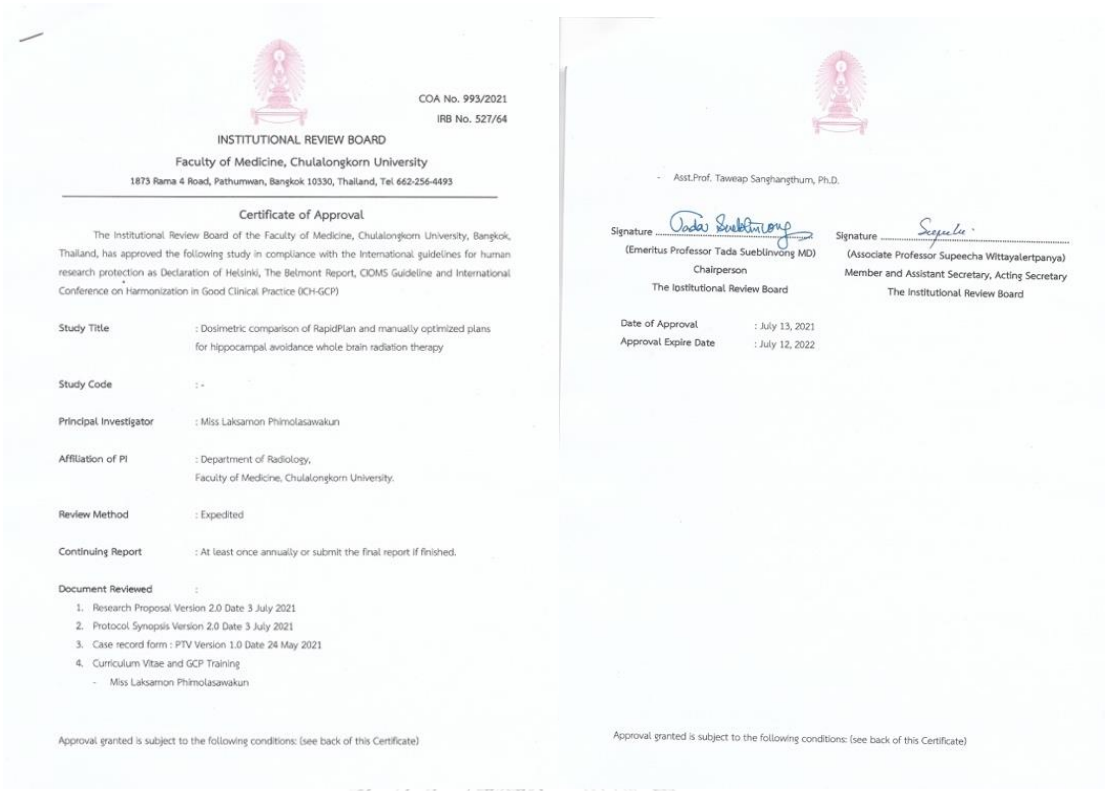
3.10 Expected benefits

The hippocampal avoidance whole brain radiotherapy is an important technique challenge to contouring and treatment planning.

If the RapidPlan model is acceptable, the RapidPlan will alleviate a labor-intensive effort from planners and will be used in clinical treatment.

3.11 Ethical consideration

This research involves the dosimetric data of WBRT patients in King Chulalongkorn Memorial Hospital. The research proposal was approved on August 06, 2021 by Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University (IRB no.527/64). The certificate is shown in figure 3.9.



COA No. 993/2021
IRB No. 527/64

INSTITUTIONAL REVIEW BOARD
Faculty of Medicine, Chulalongkorn University
1873 Rama 4 Road, Pathumwan, Bangkok 10330, Thailand, Tel 662-256-4493

Certificate of Approval

The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, has approved the following study in compliance with the International guidelines for human research protection as Declaration of Helsinki, The Belmont Report, CIOMS Guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP)

Study Title : Dosimetric comparison of RapidPlan and manually optimized plans for hippocampal avoidance whole brain radiation therapy

Study Code : -

Principal Investigator : Miss Laksamon Phimolasawakun

Affiliation of PI : Department of Radiology, Faculty of Medicine, Chulalongkorn University.

Review Method : Expedited

Continuing Report : At least once annually or submit the final report if finished.

Document Reviewed :

1. Research Proposal Version 2.0 Date 3 July 2021
2. Protocol Synopsis Version 2.0 Date 3 July 2021
3. Case record form : PTV Version 1.0 Date 24 May 2021
4. Curriculum Vitae and GCP Training
   - Miss Laksamon Phimolasawakun

Approval granted is subject to the following conditions: (see back of this Certificate)

- Asst.Prof. Taweap Sanghangthum, Ph.D.

Signature .....
(Emeritus Professor Tada Sueblinvong MD)
Chairperson
The Institutional Review Board

Signature .....
(Associate Professor Supeecha Wittayalertpanya)
Member and Assistant Secretary, Acting Secretary
The Institutional Review Board

Date of Approval : July 13, 2021
Approval Expire Date : July 12, 2022

Approval granted is subject to the following conditions: (see back of this Certificate)

Figure 3.9 The certificate of approval from ethic committee of Faculty of Medicine, Chulalongkorn University.

CHAPTER 4
RESULTS

The results of this study on each technique are summarized in table 4.1. The examples of dose-volume histograms of IMRT and VMAT are presented in figure 4.1. (The raw data are presented in Table A1. and Table A2.)

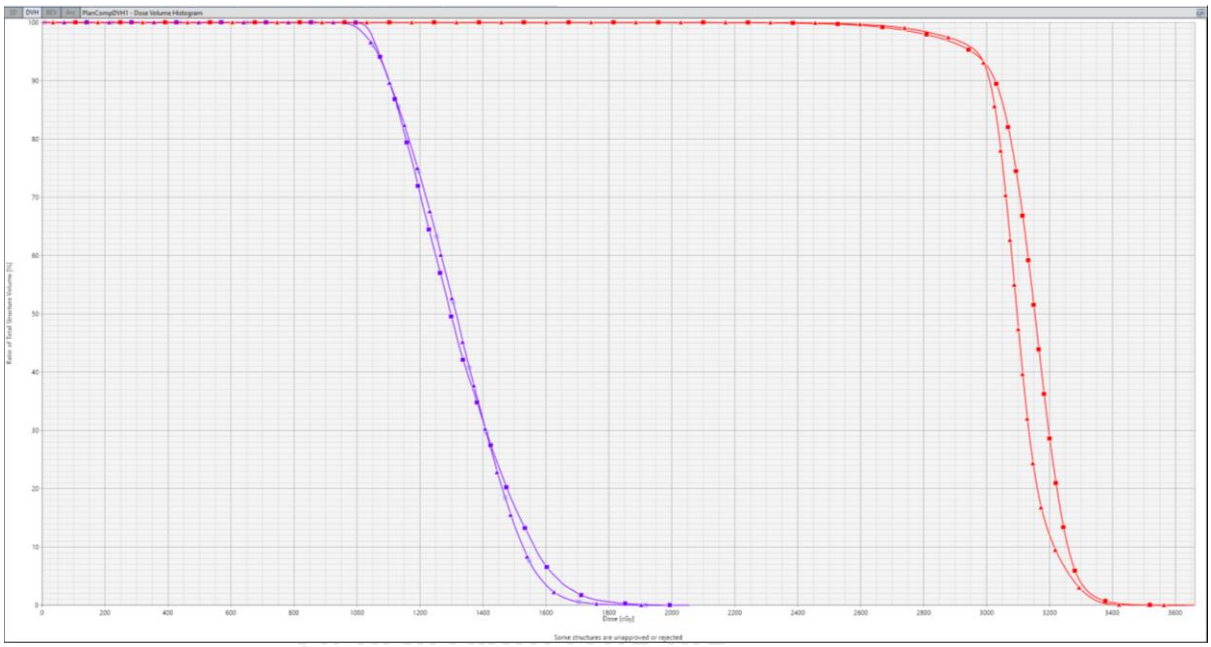


Figure 4.1 The example of a dose-volume histogram of HA-WBRT plans for manual plan and RapidPlan. The purple line represents the hippocampus, the red line represents the whole brain PTV. The triangle represents a manual plan and the square represents RapidPlan.

Table 4.1 The average results of dosimetric comparison between manually optimized plans and RapidPlan in HA-WBRT.

Parameters	Manual		RapidPlan		p-value
	Mean	SD	Mean	SD	
PTV					
Conformity Index	1.03	0.06	0.98	0.04	<0.01
Homogeneity Index	0.28	0.07	0.18	0.04	<0.01
$D_{98\%}$ (Gy)	25.83	1.86	27.69	0.98	<0.01
$D_{2\%}$ (Gy)	34.25	1.02	32.97	0.34	<0.01
Hippocampus					
$D_{100\%}$ (Gy)	8.72	0.55	9.25	0.35	0.01
D_{max} (Gy)	14.42	1.23	15.66	1.29	0.06
D_{mean} (Gy)	11.79	0.66	12.06	0.58	0.35
Lt.optic nerve					
D_{max} (Gy)	29.92	2.89	28.98	1.04	0.44
Rt.optic nerve					
D_{max} (Gy)	30.66	2.42	28.99	1.85	0.12
Lt.len					
D_{max} (Gy)	10.47	1.88	12.41	2.23	0.07
Rt.len					
D_{max} (Gy)	10.51	1.56	11.43	1.45	0.46

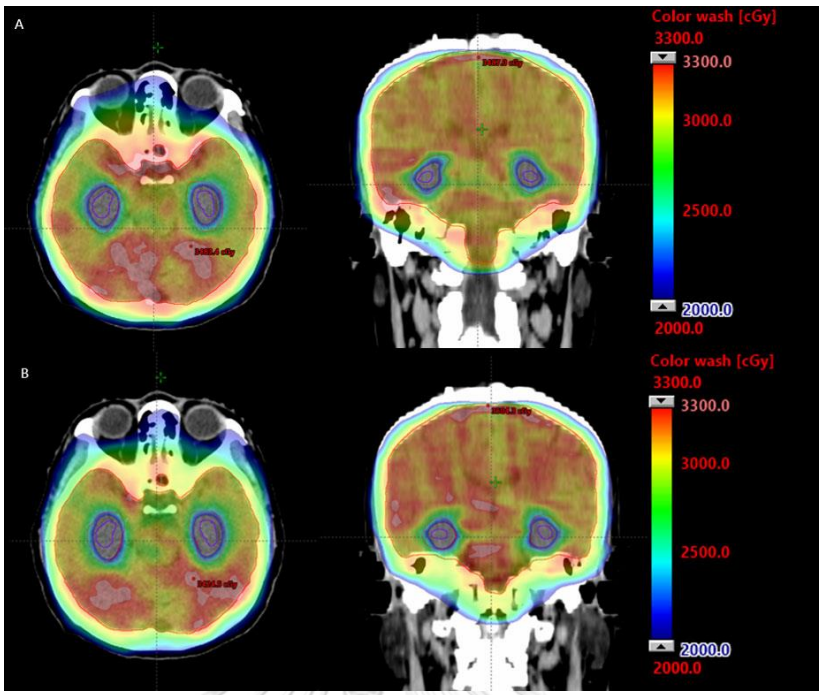


Figure 4.2 The dose color wash comparison of HA-WBRT plans for (A) Manual and (B) RapidPlan.

4.1 Planning Target Volume

The typical dose distributions in a color wash of both optimizations are shown in Figure 4.2. The blue color represents low dose area and the red represents high dose area. In the present study, all treatment plans had a maximum dose less than 37.50 Gy as per RTOG 0933 protocol and $D_{90\%}$ of PTV in both techniques was higher than the prescribed dose. The result demonstrated that both manual and RapidPlan achieved satisfactory dose distribution to the target volume. However, the $D_{98\%}$ of PTV of RapidPlan (27.69±0.98 Gy) was slightly better than manual plans (25.83±1.86 Gy). The comparison of $D_{98\%}$ is shown in figure 4.3.

Based on HI, it was found that the average value of manual plans was 0.28±0.07 and RapidPlan was 0.18±0.04. The difference between the two techniques was statistically significant ($p < 0.05$). From this data, RapidPlan gave a significantly better uniformity of dose distribution in the target volume than manual plans. The comparison of HI is shown in figure 4.4.

The CI was found that the average value of manual plans was 1.03±0.06 and RapidPlan was 0.98±0.04. The difference between these two techniques was statistically significant ($p<0.05$). From this data, RapidPlan showed slightly better conformity of dose distribution in the target volume than manual plans. The comparison of CI is shown in figure 4.4.

The $D_{2\%}$ showed that the average value of manual plans was 34.25±1.02 Gy and RapidPlan was 32.97±0.34 Gy. The difference between these two techniques was statistically significant ($p<0.05$). From this data, RapidPlan can be better reduced the maximum dose than manual plans. The comparison of $D_{2\%}$ is shown in figure 4.3.

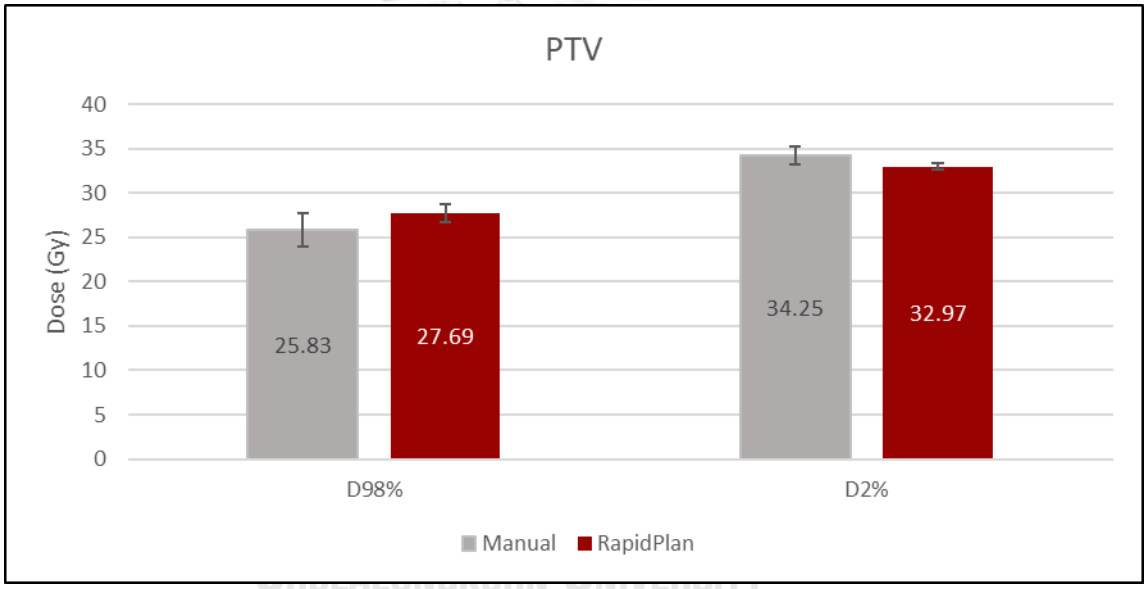


Figure 4.3 Comparison of $D_{98\%}$ and $D_{2\%}$ of PTV between manual plans and RapidPlan.

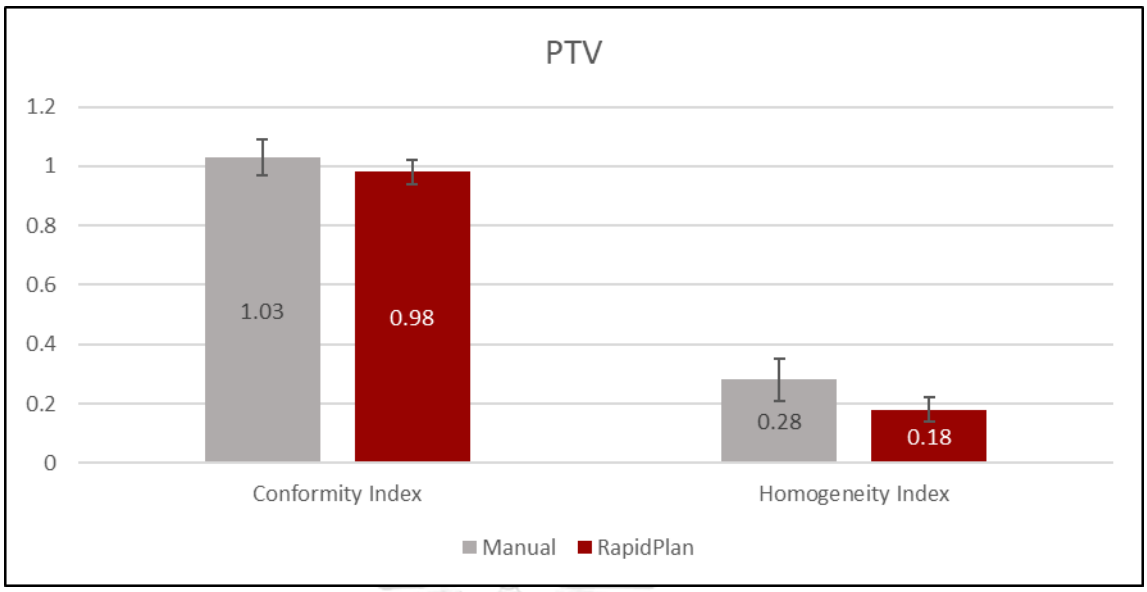


Figure 4.4 Comparison of HI and CI of PTV between manual plans and RapidPlan.

4.2 Hippocampus

Based on hippocampus maximum dose, manual plans (14.42±1.23 Gy) had slightly lower D_{max} of the hippocampus compared to RapidPlan (15.66±1.29 Gy). No significant differences (p=0.06) were found between both optimizations. The mean dose of the hippocampus of manual plans and RapidPlan were 11.79±0.66 Gy and 12.06±0.58 Gy, respectively. For minimum dose to hippocampus, $D_{100\%}$ of RapidPlan and manual plans were 9.25±0.35 Gy and 8.72±0.55 Gy, respectively. This result of the minimum dose was found that the manual plans can be better spared than RapidPlan. The comparison of $D_{100\%}$, D_{max} and D_{mean} are shown in figure 4.5.

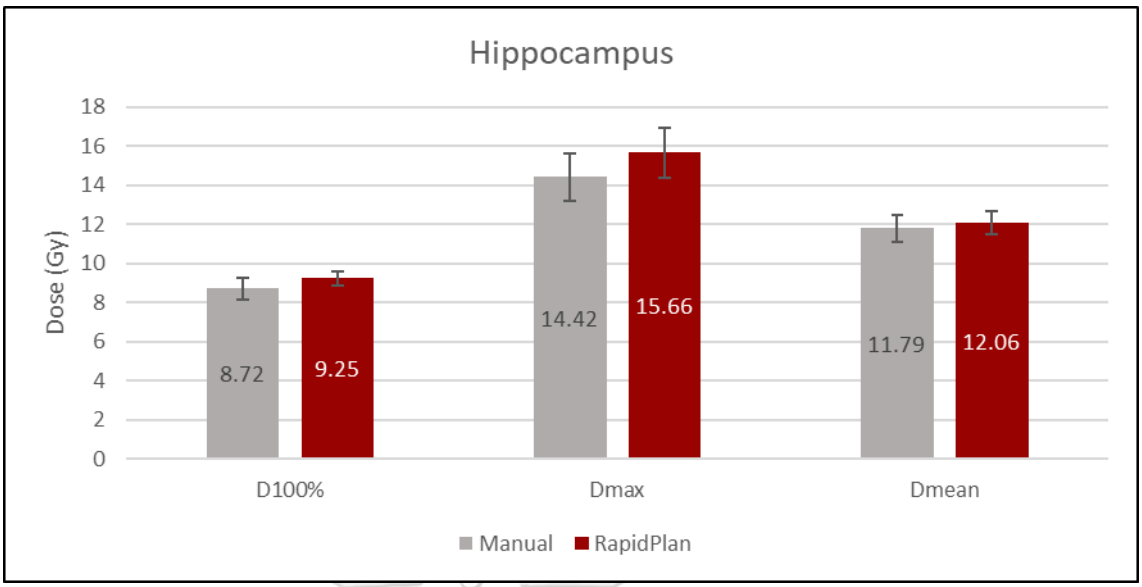


Figure 4.5 Comparison of $D_{100\%}$, Dmax and Dmean of the hippocampus between manual plans and RapidPlan.

4.3 Optic nerves and lenses

The results of optic nerves and lenses from Table 4.1. Only six cases were possible to collect because the optic nerves and lenses were not contoured in some cases.

The average maximum dose to right optic nerve and left optic nerve in manual plans were 30.66±2.42 Gy and 29.92±2.89 Gy, *respectively. For RapidPlan, the average* D_{max} *to right optic nerve and left optic nerve were 28.99*±1.85 *Gy and 28.98±04* Gy, respectively. The comparison of D_{max} and D_{mean} of optic nerves is shown in figure 4.6 and figure 4.7.

In both lenses, manual plans demonstrated *lower maximum dose and mean dose compared to RapidPlan.* The comparison of D_{max} and D_{mean} of lenses is shown in figure 4.8 and figure 4.9.

Likewise, RapidPlan demonstrated a lower maximum dose compared to manual plans in optic nerves. By the way, there are no significant differences found between both *optimizations.*

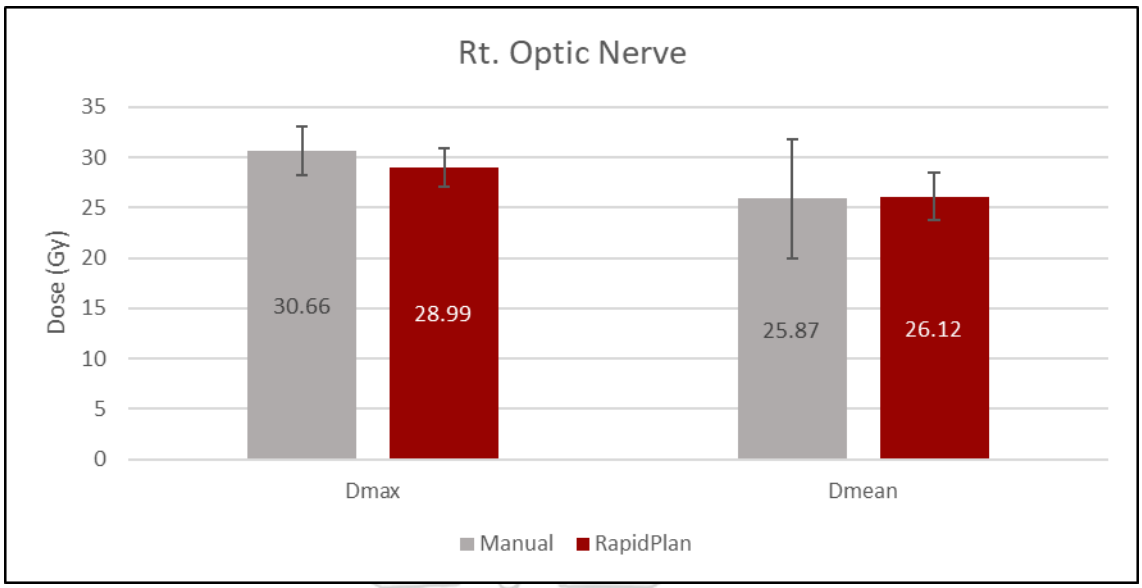


Figure 4.6 Comparison of D_{max} and D_{mean} of the right optic nerve between manual plans and RapidPlan.

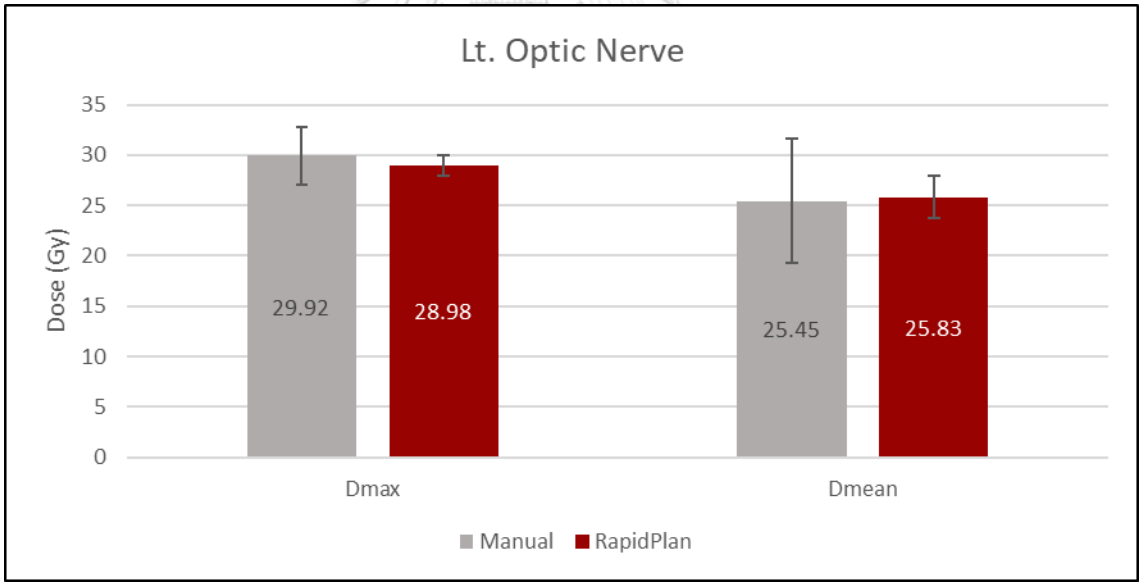


Figure 4.7 Comparison of D_{max} and D_{mean} of the left optic nerve between manual plans and RapidPlan.

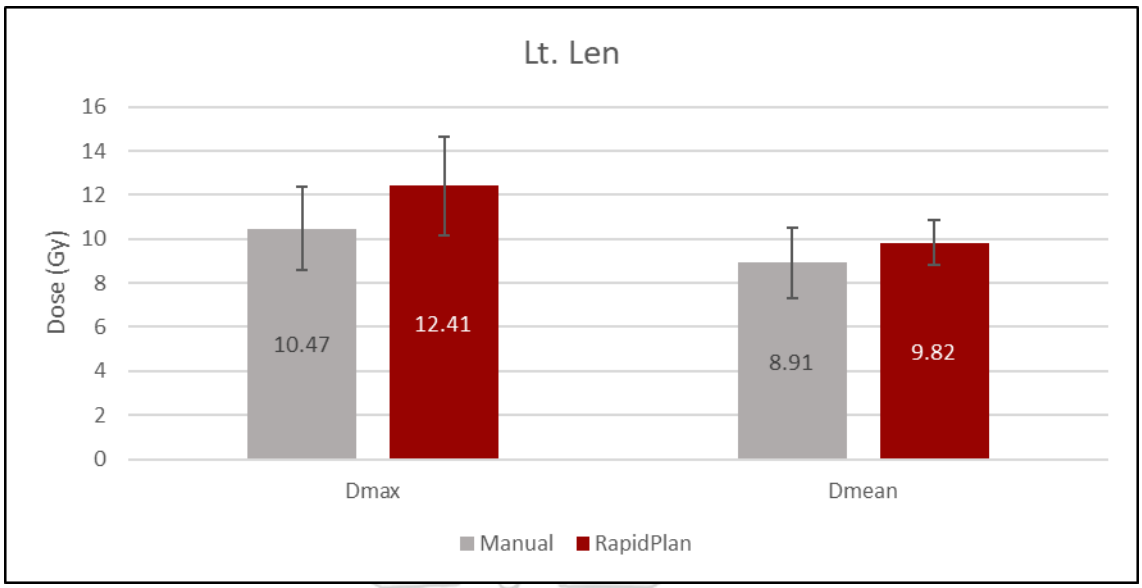


Figure 4.8 Comparison of D_{max} and D_{mean} of the left len between manual plans and RapidPlan.

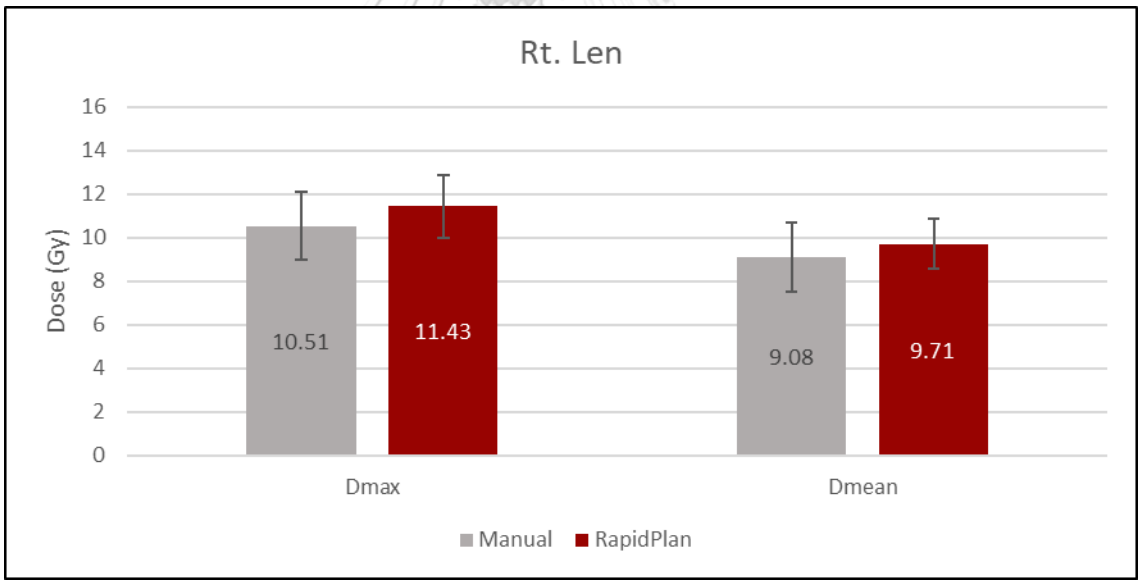


Figure 4.9 Comparison of D_{max} and D_{mean} of the right len between manual plans and RapidPlan.

CHAPTER 5
DISCUSSION AND CONCLUSION

5.1 DISCUSSION

Several studies[1][2] have assessed the comparison of dosimetric in HA-WBRT and the association between radiation doses to the hippocampus. Each study had different treatment techniques such as entering the fields, optimization, and angles of the collimator. Overall, it can be concluded that VMAT plans can reduce the dose to the hippocampus better than IMRT plans. Therefore, the VMAT technique was chosen for this study, which is widely used for HA-WBRT planning in King Chulalongkorn Memorial Hospital.

According to table 4.1, both manually optimized plan and RapidPlan have hippocampus dose and OARs dose qualified in RTOG 0933 criteria. The manual plan shows slightly better results in the hippocampus compared to RapidPlan, which is probably because the HA-WBRT plan is complex and difficult. On the other hand, RapidPlan is found to do significantly better at PTV in terms of target coverage, CI, HI, and $D_{2\%}$. However, the RapidPlan optimization can be adjusted during plans to make the hippocampus dose better in each case. The optimization process in each case takes around seven minutes which saves a lot of time and facilitates the planner.

This thesis has limitations in the number of cases. Only ten cases were chosen for the comparison between the manual plan and RapidPlan. It was originally supposed to be a case that was not trained by the RapidPlan model, but due to the very limited number of HA-WBRT cases, the author obtained eight new cases, making the other two cases were trained in the RapidPlan model. Another limitation was some of the cases that have been used in clinically tested have not drawn contour optic nerves and lenses, allowing table 4.1 in the optic nerves section and lens to be collected in only 6 cases. In some cases, the radiation oncologists did not contour the optic nerves, which may be due to the dose in RTOG 0933 criteria. A maximum dose of optic nerves is defined as ≤ 37.5 Gy, which is the same criteria as $D_{2\%}$ in PTV.

Therefore, if the PTV dose can pass the RTOG 0933 criteria, then the optic nerves should also pass.

In a dosimetric study presented by J. Krayenbuehl et al.[22], ten HA-WBRT patients were collected for automated radiotherapy planning. All cases were planned with 4 arcs VMAT techniques. The results showed a significant improvement in the dose compared to RTOG 0933 criteria. The $D_{98\%}$ of PTV was 25.8 Gy and the $D_{2\%}$ of PTV was 33.5 Gy. This dose is similar to RapidPlan in our study. For hippocampus dose, the minimum and maximum doses in this study were lower than our study. This could be explained by the different optimization in the auto planning programs. However, it concludes that automated treatment planning for HA-WBRT was able to fulfill all the constraints of RTOG 0933 criteria.

Another study by Shuo Wang et al.[21] performed the Pinnacle Auto-Planning on HA-WBRT treatment planning. Ten patients were generated by 9-field IMRT and 2-coplanar VMAT. For the PTV, the results showed the Auto-VMAT plans had a $D_{2\%}$ of 35.12 Gy, $D_{98\%}$ of 26.62 Gy. The PTV dose in our study is better than in this study. For the hippocampus, $D_{100\%}$ was 9.22 Gy for lt. hippocampus, and 9.33 Gy for rt. hippocampus. The maximum dose was 16.07 Gy for lt. hippocampus, and 16 Gy for rt. Hippocampus. The minimum dose in this study is similar to our study but the maximum dose in our study is better than Shuo Wang study. The differences of dosimetric could be explained by techniques and optimization models. Anywise, the auto planning generates acceptable plans by RTOG 0933 criteria without time-consuming planning process.

5.2 CONCLUSION

For HA-WBRT in the VMAT technique, RapidPlan shows better PTV coverage and presents a significantly conform dose to the target than manually optimized plans. Although manual plans are slightly better in the hippocampus than RapidPlan, there are no significant differences between both optimized techniques so the RapidPlan can use in clinical and slightly adjust for well-optimized plans.

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APPENDIX

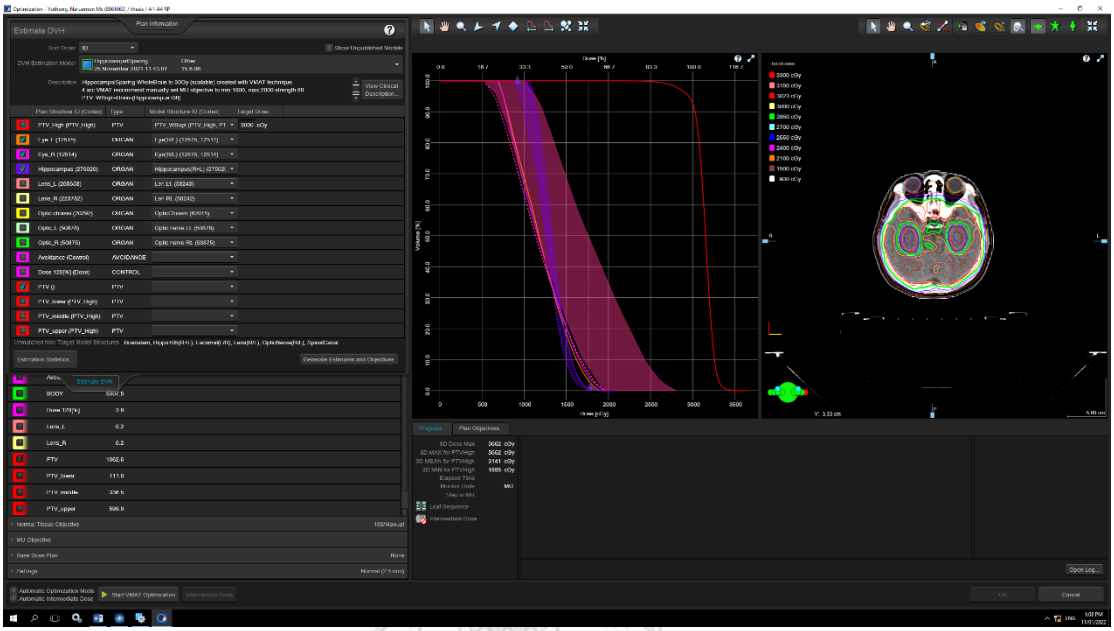

Figure A1. RapidPlan optimization window.

Table A1. The Dosimetric data of manual plans.

	PTV				Hippocampus			Lt.optic nerve & chiasm		Rt.optic nerve & chiasm		Lt.lens		Rt.lens	
Pt. No.	D98% (cGy)	D2% (cGy)	HI	CI	D100% (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)
1	2603.70	3362.90	0.25	1.03	837.30	1442.70	1198.60	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	2770.30	3337.70	0.19	0.97	906.40	1537.50	1233.40	3078.80	2950.20	3218.40	2994.70	1022.10	933.90	1083.00	955.00
3	2354.20	3555.30	0.40	0.98	775.60	1247.30	1048.00	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4	2777.20	3463.10	0.23	1.01	897.20	1437.30	1209.80	3371.50	3198.60	3343.10	3150.00	989.00	878.20	1013.90	871.40
5	2519.00	3295.00	0.26	0.96	831.60	1435.50	1198.90	3237.90	3116.60	3239.80	3159.20	1347.30	965.20	1277.40	1073.40
6	2769.10	3343.90	0.19	1.05	958.80	1659.00	1288.20	2606.90	2171.50	2720.00	2310.20	906.90	768.10	873.50	746.10
7	2814.10	3580.60	0.26	1.12	901.70	1488.30	1200.90	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8	2384.90	3406.40	0.34	1.12	820.60	1396.50	1132.40	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
9	2398.70	3535.20	0.38	1	917.80	1264.70	1137.40	2788.40	1740.70	2864.30	1775.60	1184.40	1125.50	1161.70	1091.20
10	2440.00	3368.40	0.31	1.05	877.70	1515.90	1143.30	2870.80	2093.80	3007.60	2132.70	834.90	675.20	894.80	713.00
Mean	2583.12	3424.85	0.28	1.03	872.47	1442.47	1179.09	2992.38	2545.23	3065.53	2587.07	1047.43	891.02	1050.72	908.35
Max	2814.10	3580.60	0.40	1.12	958.80	1659.00	1288.20	3371.50	3198.60	3343.10	3159.20	1347.30	1125.50	1277.40	1091.20
Min	2354.20	3295.00	0.19	0.96	775.60	1247.30	1048.00	2606.90	1740.70	2720.00	1775.60	834.90	675.20	873.50	713.00
STD.	186.00	101.81	0.07	0.06	54.91	122.61	66.19	288.61	617.75	242.50	591.94	188.50	157.59	156.09	160.44

Table A2. The Dosimetric data of RapidPlan.

	PTV				Hippocampus			Lt.optic nerve & chiasm		Rt.optic nerve & chiasm		Lt.lens		Rt.lens	
Pt. No.	D98% (cGy)	D2% (cGy)	HI	CI	D100% (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)	Dmax (cGy)	Dmean (cGy)
1	2845.50	3321.50	0.16	1.00	941.30	1733.90	1241.70	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	2744.10	3307.20	0.19	0.96	966.40	1448.90	1184.50	2938.80	2764.70	2969.90	2771.40	1223.60	990.00	1118.20	1000.40
3	2878.60	3309.90	0.14	0.96	935.80	1702.00	1265.20	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4	2828.00	3215.80	0.13	0.93	923.40	1669.70	1267.00	2878.60	2777.40	2856.70	2764.50	1174.20	944.00	1132.50	856.90
5	2687.10	3325.30	0.21	0.93	858.20	1366.10	1083.40	2905.60	2637.00	2984.90	2674.80	1616.00	1033.80	985.30	866.40
6	2778.60	3293.60	0.17	0.98	923.30	1710.60	1264.40	2703.00	2221.80	2548.10	2152.70	994.30	818.60	1143.30	967.30
7	2925.40	3269.00	0.11	1.03	923.60	1555.80	1196.20	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8	2630.70	3286.50	0.22	1.03	877.90	1505.80	1160.90	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
9	2674.90	3333.50	0.22	1.00	969.00	1496.70	1224.50	2981.40	2641.30	2965.20	2715.90	1074.10	976.10	1067.20	964.70
10	2698.70	3304.50	0.20	0.97	933.60	1466.70	1176.50	2980.50	2457.30	3068.60	2589.80	1362.20	1128.70	1414.20	1167.80
Mean	2769.16	3296.68	0.18	0.98	925.25	1565.62	1206.43	2897.98	2583.25	2898.90	2611.52	1240.73	981.87	1143.45	970.58
Max	2925.40	3333.50	0.22	1.03	969.00	1733.90	1267.00	2981.40	2777.40	3068.60	2771.40	1616.00	1128.70	1414.20	1167.80
Min	2630.70	3215.80	0.11	0.93	858.20	1366.10	1083.40	2703.00	2221.80	2548.10	2152.70	994.30	818.60	985.30	856.90
STD.	97.84	34.25	0.04	0.04	34.63	129.28	58.45	103.81	211.37	184.65	234.46	223.07	102.42	144.84	112.79

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