THE EFFECT OF CONTRAST AGENTS ON DOSE CALCULATION IN CONFORMAL RADIOTHERAPY PLANNING USING COMPUTED TOMOGRAPHY FOR TUMORS AT DIFFERENT ANATOMICAL REGIONS

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ABSTRACT

The purpose of this study was to evaluate the effect of contrast agents on dose calculation in 3-Dimensional Conformal Radiotherapy (3D-CRT) for brain, thorax and upper abdomen regions in Ramathibodi Hospital, Thailand. Five, six and four cancer patients of the brain, thorax and upper abdomen regions were studied, respectively. Two sets of CT images of each patient were taken from the same position before and after IV contrast agent injection. A treatment plan was approved by radiation oncologists for each patient in study. A “without contrast agent CT images” set was simulated for the thorax and the upper abdomen regions by measuring the density of the organs or regions that were filled with a contrast agent (in real without contrast agent CT image) then overridden by measured density in the “with contrast agent CT images”. The approved treatment plan was copied to “without contrast agent CT images” and dose was calculated and then treatment plan was copied to “with contrast agent CT images” with the same monitor units and the dose was calculated again. The doses calculated from two treatment plans were compared with regard to tumor volume and organs at risk by paired sample t-test. Gamma evaluation (3%/3mm) was used to evaluate the differences in dose distribution between the two treatment plans. The results for doses of tumor volume and organs at risk were not significantly different between with and without contrast agent CT image for brain, thorax and upper abdomen regions ($p>0.05$), except for the heart organ in the thorax region ($p<0.05$) but the dose differences were less than 1% compared to doses calculated from “without contrast agent CT images”. Dose distributions between the two sets of CT images were not different (percent pixel pass > 95% and mean gamma value < 0.5). From these results, using contrast agent at the time of CT simulation does not significantly affect dose calculation in 3D-CRT.

KEY WORDS: CONFORMAL RADIOTHERAPY/ CONTRAST AGENT/ TREATMENT PLANNING/ DOSE CALCULATION

53 pages

ผลของสารทึบรังสีต่อการคำนวณปริมาณรังสีจากแผนการรักษาแบบสามมิติ โดยใช้เครื่องเอกซเรย์คอมพิวเตอร์ สำหรับมะเร็งในตำแหน่งต่างๆ

THE EFFECT OF CONTRAST AGENTS ON DOSE CALCULATION IN CONFORMAL RADIOTHERAPY PLANNING USING COMPUTED TOMOGRAPHY FOR TUMORS AT DIFFERENT ANATOMICAL REGIONS

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บทคัดย่อ

วัตถุประสงค์ของการศึกษาในครั้งนี้เพื่อประเมินผลกระทบที่เกิดจากสารทึบรังสีที่ใช้ร่วมในการสร้างภาพเอกซเรย์คอมพิวเตอร์ต่อการคำนวณปริมาณรังสีในการวางแผนการรักษาแบบสามมิติ โดยศึกษาแบบย้อนหลังในผู้ป่วยมะเร็งบริเวณศีรษะ ทรวงอก และช่องท้องส่วนบนของโรงพยาบาลรามาธิบดีจำนวน 5, 6 และ 4 รายตามลำดับ โดยคัดเลือกผู้ป่วยที่จำลองการรักษาด้วยเครื่องเอกซเรย์คอมพิวเตอร์ซึ่งสร้างภาพทั้งก่อนและหลังการฉีดสารทึบรังสี และจำลองภาพเอกซเรย์คอมพิวเตอร์ที่ไม่มีสารทึบรังสีสำหรับบริเวณทรวงอกและช่องท้องส่วนบน วางแผนการรักษาในภาพเอกซเรย์คอมพิว์เตอร์ทั้งสองชุดโดยใช้แผนการรักษาที่ได้รับการอนุมัติจากแพทย์แล้วและคำนวณปริมาณรังสี โดยกำหนดค่า Monitor units ให้เท่ากันทั้งสองแผนการรักษา เปรียบเทียบประมาณรังสีที่ได้จากทั้งสองแผนการรักษาทั้งในก้อนมะเร็งและอวัยวะสำคัญด้วย Pairs sample t-test และใช้ Gamma evaluation ด้วยเกณฑ์ 3%/3 mmในการเปรียบเทียบการกระจายของปริมาณรังสี ผลการศึกษาพบว่าปริมาณรังสีระหว่างแผนการรักษาของภาพเอกซเรย์คอมพิวเตอร์ที่มีและไม่มีสารทึบรังสีทั้งในก้อนมะเร็งและอวัยวะสำคัญไม่แตกต่างกันอย่างมีนัยสำคัญ ($p>0.05$) ยกเว้นที่หัวใจในบริเวณทรวงอก ($p<0.05$) แต่ความแตกต่างของปริมาณรังสีน้อยกว่า 1% ผลจาก Gamma evaluation พบว่าการกระจายของปริมาณรังสีจากทั้งสองแผนการรักษาไม่แตกต่างกันด้วยค่าเปอร์เซนต์ของพิกเซลที่ผ่านเกณฑ์มากกว่า 95% และค่า Gamma เฉลี่ยน้อยกว่า 0.5 ทุกการทดสอบ ดังนั้นจากผลการศึกษาจึงกล่าวได้ว่าการใช้ภาพเอกซเรย์คอมพิวเตอร์ที่มีสารทึบรังสีในการวางแผนการรักษานั้นไม่ส่งผลต่อการคำนวณปริมาณรังสีในการวางแผนการรักษาแบบสามมิติ

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LIST OF ABBREVIATIONS

Abbreviation	Terms
3D	Three dimension
3D-CRT	Three dimension conformal radiotherapy
$BaSO_4$	Barium sulfate
BEV	Beam Eye View
cm	Centimeter
cm^3	Cubic centimeter
CT	Computed tomography
DRRs	Digitally reconstructed radiographs
DTA	Distance to agreement
DVH	Dose Volume Histogram
g	Gram
Gy	Gray
IMRT	Intensity Modulated Radiotherapy
kg	Kilogram
kVp	Kilo voltage peak
mA	Milliampere
mAs	Milliampere second
mg	Milligram
mgI	Milligram iodine
min	Minute
mL	Milliliter
mm	Millimeter
MRI	Magnetic resonance imaging
MU	Monitor units
MV	Megavoltage
No.	Number

LIST OF ABBREVIATIONS (cont.)

Abbreviation	Terms
OARs	Organs at risk
PDD	Percentage depth dose
PET	Positron Emission Tomography
PTV	Planning arget volume
secs	Seconds
SD	Standard eviation
SRS	Sterotactic Radiosurgery
SRT	Sterotactic Radiotherapy
SSD	Source to skin distance
TERMA	Total energy released per unit mass
TPS	Treatment planning system
HUs	Hounsfield units

CHAPTER I
INTRODUCTION

Computed tomography (CT) images are primary images for radiotherapy treatment planning due to providing the information of axial images for the internal organ, high image resolution and CT number for converting to electron density in dose calculation. The CT number is very useful for tissue inhomogeneity correction that provides more accurate calculating dose for 3D treatment planning [1].

In 3D treatment planning such as 3 Dimensional Conformal Radiotherapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT) and Sterotactic Radiosurgery/ Radiotherapy (SRS/SRT), using contrast agents during CT scanning improve the accuracy of tumor volume and organs at risk delineation. For dose calculation, CT number is converted to electron density, so using contrast agents will make the mean CT number and also the electron density increase. However using treatment delivery, contrast agents are not used therefore, the error of the dose to be irradiated in a patient might be obtained.

Therefore for more accuracy in 3D dose calculation, the study of the effect of contrast agents on the dose calculation is very significant.

In this research, we studied the effect of contrast agents on dose calculation in conformal radiotherapy planning using computed tomography in the faculty of medicine Ramathibodi hospital for brain, thorax and upper abdomen regions. The calculation of dose volume between with and without contrast agents were compared using the percentage of dose difference and statistics for analysis. Furthermore, dose distributions were evaluated using gamma evaluation method.

1.1 CT scanner and virtual Simulator [2, 3]

X-ray computed tomography (CT) scanner provides high contrast transverse image. This information is used to create a density map from correct

calculation of x-ray beam penetration. CT is the modality of choice for radiotherapy treatment planning. CT provides accurate internal and external contour including the map of electron density to dose calculation. Using CT information in radiotherapy planning helps improve the efficiency and reduce any mistakes in treatment planning.

Now a day, most radiotherapy departments have CT scanner for simulation. The advantage of using CT scanner is the production of the multiple slices which can be used in 3-D treatment planning, both visualization and dose calculation. The disadvantage is that the scout view does not account for beam divergence, which provided by simulation so Beam Eye View (BEV) including beam divergence is required. Therefore CT scanners have to include software that simulates BEV by the process known as virtual simulation and BEVs are obtained by image reconstructions are known as digitally reconstructed radiographs (DRRs).

The requirement of CT scanner as illustrated in Figure 1.1 for radiotherapy treatment planning is that the bore gantry is bigger than the one of conventional CT in order to support patient immobilization such as a breast board.

Figure 1.1 CT simulator (Phillips AcQSim).

In the process of radiotherapy in the simulation room, specified isocenter is established with reference to mark on patient's skin using virtual simulation. The

patient is placed on a CT couch and reference lines are marked. These are aligned with a set of lateral and overhead laser. Then the patient is scanned. When the scan is completed and CT data are reconstructed, image data are sent to radiotherapy treatment planning system. The tumor volume and organ at risk are delineated. Next, isocenter is placed in the tumor site that related to the coordinate between reference marker and isocenter. The virtual simulation software estimates the laser offsets to move the lasers by the same amount as x, y, z shifted from reference marker position to isocenter position. Finally, the isocenter on patient skin is marked with permanent marker for setup.

CT simulation data and isocenter position are sent to radiotherapy treatment planning system in order to plan and calculate dose in the cancer patient.

1.2 The importance of CT Number on dose calculation [3, 4]

The most important radiation interaction with matters in radiotherapy is Compton interactions. Probability of Compton interactions is independent to atomic number (Z) but depends on the number of free electrons. When electron density (numbers of electrons per cm^3) increases, the probability of Compton interactions will increase. Most materials except hydrogen can be considered as having approximately the same number of electrons per gram. Thus Compton mass attenuation coefficient (σ/ρ) is nearly the same of all materials. But each material has different physical density (g/cm^3) so difference in x- ray attenuation. For example, bone and muscle have nearly the same number of electron per gram which are 3.36×10^{23} and 3.00×10^{23}, respectively. But, the physical density of bone and muscle are quite different. If the physical density of bone is assumed to be 1.85 g/cm^3 and that of muscle is 1 g/cm^3, thus they have difference in electron density (numbers of electron $/cm^3$), and then the attenuation produced by 1 cm of bone will be equivalent to that produced by 1.65 cm of muscle. The relationship between electron density (numbers of electrons/cm^3) and physical density can be written as

electron density *(numbers of electrons/cm^3)* = ***electron content*** *(numbers of electrons/g)* × ***physical density*** *(g/cm^3)* ……..(1)

So, when physical density increased electron density will increased.

For radiotherapy treatment planning, CT images are reconstructed to 3D images and CT number is converted to electron density in dose calculation for treatment planning system. And electron density is representation of photon attenuation for each tissue in radiotherapy. When CT number value increases, mean value of electron density will increase. Therefore, CT number is very important in 3D dose calculation.

The conversion of CT number to electron density refers to the conversion of attenuation in diagnostic x-ray energy to radiotherapy x-ray energy which is the relationship curve or table between CT number and electron density. This will calculate the CT calibration line which described in the following topic.

1.3 Obtaining CT calibration lines [3]

A data table of CT calibration line is used to compute electron density from CT number in radiotherapy treatment planning computers. Some radiotherapy treatment planning computers require data for mass density (physical density) versus CT number and conversion to electron density then electron density is computed in the system. Obtaining CT calibration lines was measured in various materials such as bone, soft tissue, lung and solid water. Usually, the materials are shaped into cylinders of diameter about 2 cm and placed in a cylindrical phantom of diameter about 30 cm. Various material are scanned with CT scanner and are measured CT number values.

Shape of phantom should be cylindrical or like patient anatomy to avoid CT image distortion due to artifacts from reconstruction. An appropriate phantom is made from solid water or tissue equivalent as shown in Figure 1.2. The samples are placed individually, for avoiding cross talk from another sample that affect on the CT number recorded in the other sample position. And sample positions have to position across scan plane in order to quantify the small deviation in CT number value with position versus electron density. A CT number to electron density line is illustrated in Figure 1.3. The CT number varies from different scanners because of the change in tube energy. In Figure 1.4, representative bone line depends on scanner energy. When

energy increases, the slope of the curve will decrease. Some radiotherapy treatment planning computers require CT number plus 1000 as an offset of input data. A CT calibration line used in radiation treatment planning computers for dose calculations is shown in Figure 1.5.

Figure 1.2 Phantom (Gammex RMI 467) for CT calibration which inserted samples of known mass and electron density.

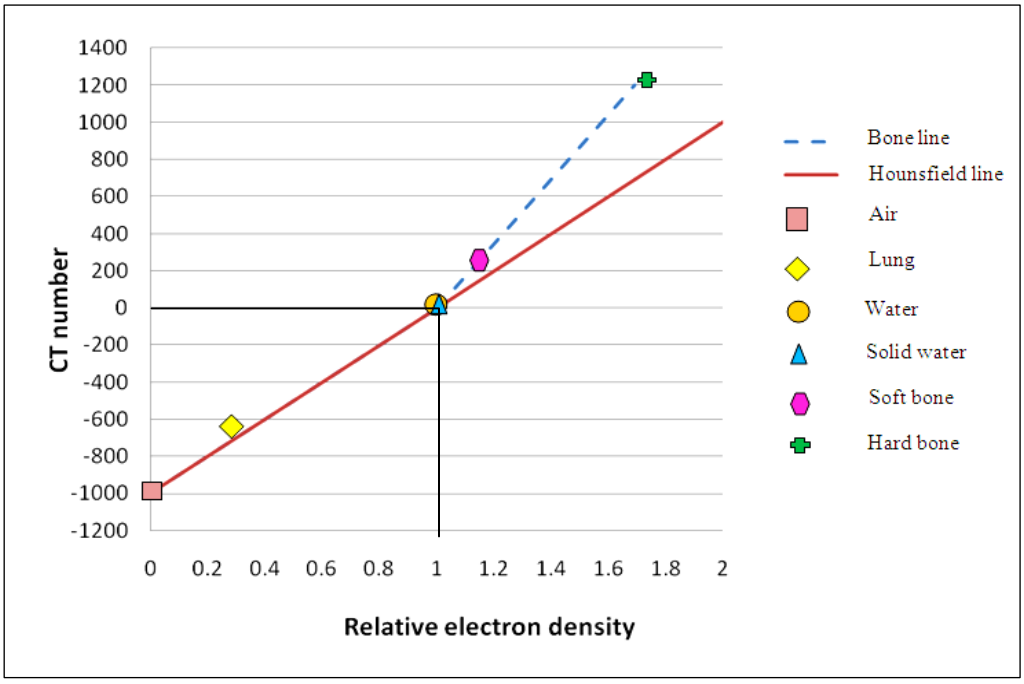


Figure 1.3 Curve of CT number (x- axis) versus electron density (y-axis) measured on a Phillips CT scanner at energy 71 keV (120 kVp).

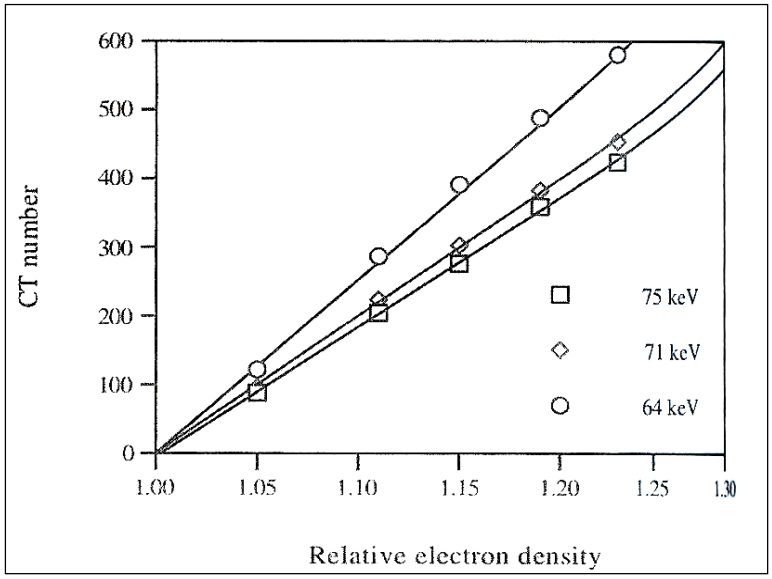


Figure 1.4 Curve of CT number (x- axis) versus electron density (y-axis) for liquid bone sample (K_2HPO_4) at three different energies measured on a Phillip CT scanner.

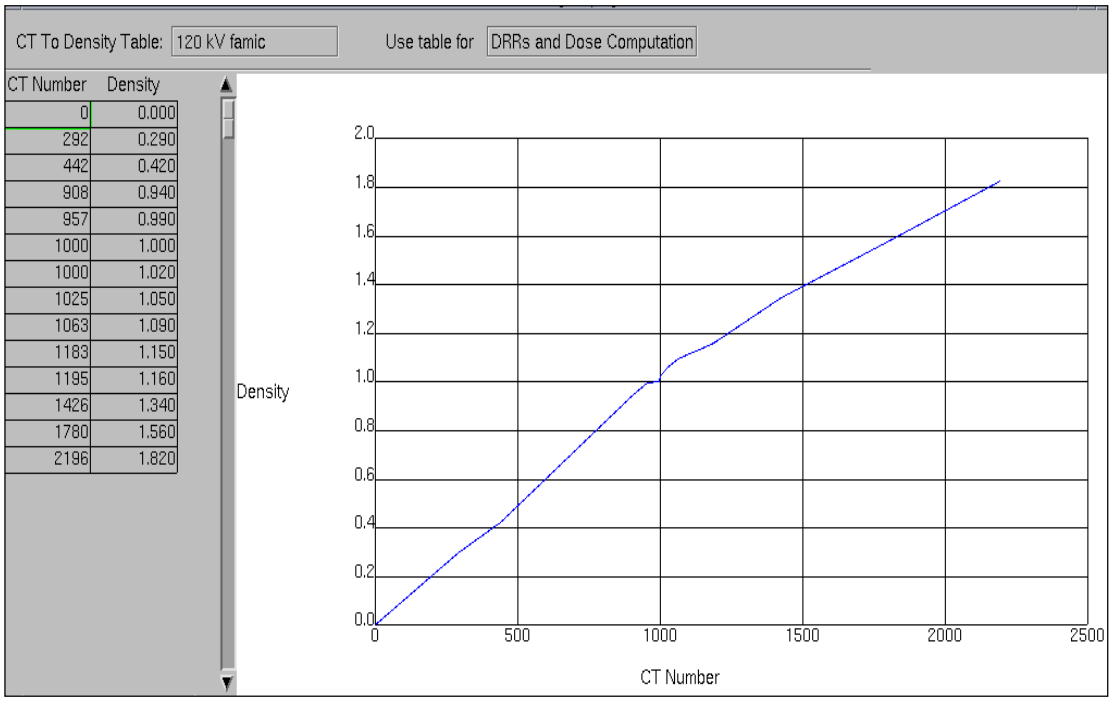


Figure 1.5 CT number to density data used in radiotherapy computer treatment planning. The CT number +1000 is shown on x-axis and mass density represents on y-axis. All data were collected using the RMI CT phantom on Philips CT scanner (Philips, Mx 8000 IDT).

CT number is linear correlation with linear attenuation coefficient that represents in mass density (Figure 1.5). Although CT number relate with mass density, but the relation is not linear through every mass density, because the variation of atomic number in tissue that affect to portion of x-ray attenuation from compton scattering effect and photoelectric effect. In Figure 1.5, shown linear correlation between lung and soft tissue but not linear between lung and bone.

Variation of x-ray spectrum is a little effect to soft tissue calibration line but is more effect to slope of relationship between CT number and electron density of bone because photoelectric absorption will more occur when increase atomic number of tissue and low x-ray energy.

1.4 Relation between CT number and Electron Density [3, 5]

Megavoltage photon interactions in radiotherapy interact with tissue the most interaction is Compton interactions, and dose calculation require relation of electron density. CT scan can obtain the relative electron density for tissue of interest from CT images or scan information. CT numbers are defined in Hounsfield units (HU) and relationship between CT number and the linear attenuation coefficient can find by the following equation:

$$CT\ number = 1000\left(\frac{\mu - \mu_w}{\mu_w}\right) \qquad \text{.....(2)}$$

where μ is the linear attenuation coefficient for tissue of interest, μ_w is the linear attenuation coefficient for water. Linear attenuation coefficient relates with electron density (ρ_e; electrons per cm^3) and total electron cross section (σ_e; cm^2 per electrons). When know about CT number value, electron density can be known.

From data in Figure 1.3, relationship between CT number and electron density can be written as

$$\rho_e^w = R_\gamma\left(\frac{1}{1000}N_{CT}\right)+1 \qquad \text{.....(3)}$$

where R_γ is experimental regression line slope for material of difference atomic number, N_{CT} is CT number and ρ_e^w is relative electron density of other tissue to water.

The regression equations are useful for radiotherapy treatment planning. These equations are used to convert from CT number to relative electron density that CT number depends on the x-ray tube energy. So regression equations will different for different CT scanners or different x-ray energies in the same scanner.

1.5 CT contrast agents for x-ray computed tomography [6]

CT contrast agent is the agent that used during x-ray computed tomography scan. It is made of high atomic number materials such as iodine or barium sulfate, in order to improve image contrast between organs of interest and adjacent organs. CT contrast agents can be divided into 2 groups which are

1.5.1 Barium sulfate ($BaSO_4$) usually is used in gastrointestinal system. $BaSO_4$ used in upper GI study or barium edema cannot be used for diagnostic with computed tomography scanner because too high concentration which will induce artifact to hide lesions and maybe precipitate, the effect on contrast agent cannot coat gastrointestinal cavity thoroughly. New products are improved to use in computed tomography scanner which is $BaSO_4$ with concentration of 1%-3% in form of suspension with volume about 600-800 cm^3, that will not precipitate during CT scan.

1.5.2 Iodinated contrast agent is water soluble iodine compound that can be classified in 2 types which are ionic and non-ionic. They are used for intravenous administration, oral contrast administration or enema.

Using contrast agents during x-ray computed tomography allows to improve visualizes and more accurate contouring of target tumor and organ at risks. Therefore, contrast agent is essential for radiotherapy treatment planning. But, contrast agents made from high atomic number element, that high attenuation in the range of energy for diagnostic x-ray, that effect to CT number will be increased. High CT number means high mass tissue density that effect to error on dose calculation.

1.6 Effect of contrast agent on changing CT Number

Giving contrast agents during x-ray computed tomography allow CT number increased because contrast agents are made from high atomic number agents, which increase photoelectric interaction and increase attenuation, so CT number will increase. Other than element composed to contrast agents, remain have any factor that effect to CT number as follows.

1.6.1 Barium sulfate ($BaSO_4$) contrast agents

Variation of CT number for Barium sulfate ($BaSO_4$) contrast agents occur from varying $BaSO_4$ concentration.

Ramm U et al. [7] described varying $BaSO_4$ concentration makes variation in CT number as shown in Figure 1.6.

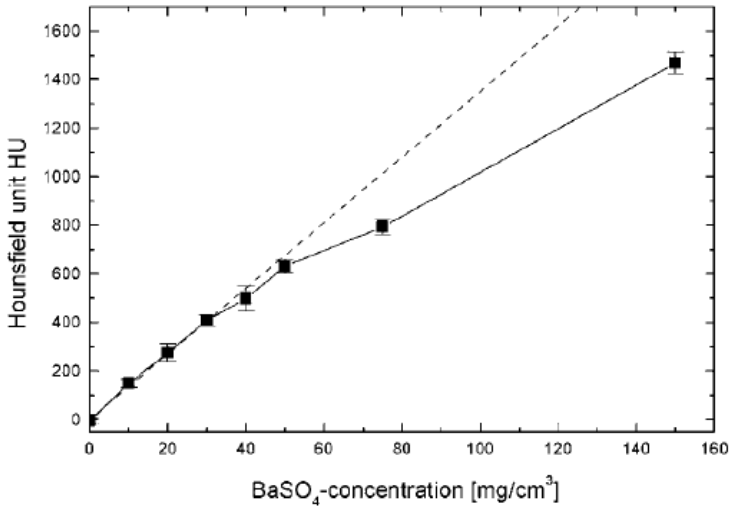


Figure 1.6 Relationship between CT number (Hounsfield Unit) and $BaSO_4$ concentration from CT scanner with 120 kVp.

In Figure 1.6, curve as shown the relationship between CT number and $BaSO_4$ concentration when increased $BaSO_4$ concentration then CT number will be increased. The deviation from linearity is due to beam-hardening effect. When, the higher atomic number agents, the x-ray beam hardening will greater.

1.6.2 Iodinated contrast agents

The change of CT number after CT contrast agents was administrated depend on [8]

1.6.2.1 Rate of injection

1.6.2.2 CT contrast agent (iodine) concentration

1.6.2.3 Delay time, after CT contrast agents was administrated to start

1.6.2.4 CT scan

1.6.2.5 Type of tissue in patient body

In addition, the change of CT number within target volume depends on metabolism of each patient and position of target in patient body.

CHAPTER II
OBJECTIVE

The objective of this study is:

To study the effect of CT contrast agents on dose calculation for brain, thorax and upper abdomen regions in 3-Dimensional Conformal Radiotherapy (3D-CRT) with Pinnacle Treatment Planning version 7.6C at Ramathibodi Hospital.

CHAPTER III
LITERATURE REVIEWS

The impact of contrast agent on dose calculation in computer treatment planning system is quite concerned because CT images are used in 3D treatment planning. Using CT contrast agents in CT simulation process is useful in tumor target and organs at risk delineation while changing CT number. Therefore studying about the effect of CT contrast agents to dose calculation is essential.

Ramm U. et al [7] studied the effect of CT contrast agents on dose calculation in water phantom for 3D treatment planning. $BaSO_4$ (micropaque) was varied in concentrations between 10 to 150 mg/cm^3 and was contained in a plastic container with diameter of 3, 6 and 9 cm. Then it was placed in a water phantom. $BaSo_4$ with oil was used in high concentration case (75-150 mg/cm^3). A midline of the water phantom was scanned by Phillips CRS 700 CT scanner with 120 kVp and 250 mAs exposure technique. The CT numbers were measured in the center of the plastic container and CT images were transferred to Helax TMS software treatment planning system. Planning was performed by a single beam with field size of 5×5 cm^2 projected to water phantom that contains $BaSO_4$ in the center. The energies of 6 and 25 MV were used. The dose was normalized at a depth of dose maximum in a volume of interest. In order to study the effect of CT contrast agents on dose calculation in clinic, two opposing photon beam and isocentric 4 field box techniques for 6 and 25 MV were used. Then the monitor units were calculated. When number of beams (4 fields box technique) increased, calculated dose difference between using with and without contrast agents decreased. Dose differences between doses calculated from with and without contrast agents CT image increase linearity with concentrations and expansion of contrast agents within water phantom. Using CT contrast agents allow accurate in

tumor and organ at risks volume delineation however safety and reliability of using CT contrast agents must be concerned. When CT number less than 500 HU was located within region of diameter less than 5 cm, dose difference between doses calculated from with and without contrast agents was less than 3%.

Choi Y. et al [8] studied the effect of CT contrast agents on IMRT dose calculation for head and neck cancer. Five head and neck cancer patients were studied. Two sets of CT images (with and without contrast agents) were scanned with 120 kVp and 150 mAs exposure technique. The concentration of 320 mgI/mL contrast agents with volume of 90 mL was administrated with delay time after injection 5 seconds and injection time was 45 seconds. Two sets of CT images were transferred to Eclipse (version 6.5), Varian, Palo Alto, CA) treatment planning system for dose calculation. First, with contrast CT images was used for tumor volume and organ at risks delineation. Varian 2100EX (120 MLC) of 6 MV with IMRT plan was performed. Objectives of plan were that the 95% within planning target volume (PTV) should received altogether prescribed dose, and the maximum and minimum dose of PTV should less than 115% and more than 95% of prescribed dose, respectively. Spinal cord had to receive dose less than 50 Gy, but if it received 45 Gy, it must be less than 5% of the spinal cord. For parotid gland had to receive dose as low as possible. Second, without contrast CT images was used with the same energy, technique and objectives as the first plan For analysis, the Wilcoxon's sighed rank test was used to distinguish the comparison result between 2 sets of CT images both with and without contrast agents for each patients. As a result, PTV70 and PTV59.5 of with contrast agents CT images were less than those of without contrast agents CT images, but PTV50.4 and dose at organ at risks were not significantly different. Due to CT contrast agents are useful for delineation, researchers concluded that considering of using with contrast agents CT image for IMRT dose calculation in head and neck cancer obtained more efficiency than considering of the accuracy of the dose calculation.

Liauw. et al. [9] studied the effect of intravenous contrast on intensity-modulated radiation therapy dose calculation for head and neck cancer. Five head and neck cancer patients were studied. Nonionic-iodinated contrast agent (Iohexol) with 300 mgI/mL concentrations, 130 mL volume, was used with 0.4 mL/secs rate of injection and 20 seconds delay time. The x-ray computed tomography was Phillips PQ

6000 scanner. From CT images, critical target volume and organ at risks were contoured. A radiotherapy treatment planning was planned by Pinnacle treatment planning system (Phillips Medical System). The aim was to study the effect of CT contrast agents with various contrast densities within blood vessel. The contrast densities were divided into 3 types; normal contrast, no contrast and maximum contrast. The results were compared with adjacent soft tissue that did not uptake contrast agents. CT contrast agents in blood vessel at normal contrast have mass density more than adjacent soft tissue which is more than 1.00 g/cm^3. The same plan conditions were used for every contrast density. Each contrast density can be described as following, normal contrast was 1.05 g/cm^3 blood vessel density, no contrast was 1.00 g/cm^3 blood vessel density and maximum contrast was 1.7 g/cm^3 blood vessel density. The results were analyzed using percent dose difference within target volume and organs at risk. When CT number increased, mass density increased. Isodose distribution for with contrast and without contrast showed no difference in dose distribution both between normal contrast and no contrast and between maximum contrast and no contrast. Mean calculated dose difference between normal contrast and no contrast was less than 0.2%, and mean calculated dose difference between maximum contrast and no contrast was less than 0.5%. In conclusion, when increased of CT number difference, dose difference between with and without contrast will increased. Intravenous contrast agents did not influence IMRT dose calculation in head and neck cancer.

Burridge NA et al. [10] studied the effect of CT contrast agents on 3D dose calculation in lung and compensated for the influence of CT contrast agents on dose calculation. Treatment planning system that used to perform treatment plan was Pinnacle^3 planning system (Phillips Medical System, Medison, WI). Three lung cancer patients were studied in this research. CT images were acquired by x-ray computed tomography (GE Medical Systems Lightspeed Plus CT scanner) for the exposure technique of 120 kVp and 210 mA. The scanning started when CT number within ascending aorta equaled 50 HU. The intravenous contrast agent (Omipaque) with 200 mL volume containing 140 mgI/mL was used. All CT images were transferred to treatment planning system. The contrast agents on CT images were simulated from without contrast agents CT images in 18 patients. Then, treatment

planning was performed on two sets of CT images by the same conditions of the plan. Monitor units were compared in the same region for both two sets of CT images. Dose difference was compared between without contrast agents and simulated contrast agents. When CT number increased, percent difference of monitor unit between with and without contrast agents increased. Dose in treatment planning calculated from with contrast agents CT images overestimated because CT contrast agents did not present at the time of treatment. The gamma index was used to assess dose distributions between plan with and without contrast agents. When monitor unit from plan with contrast agents are copied to without contrast CT image, the result showed that mean percent pixel failing within 80% isodose increased when CT number increased. In order to decrease the effect of CT contrast agents on dose calculation, researchers created method to correct for this effect by modifying CT to density line as shown in Figure 3.1. When correction method was implemented, mean percent pixel failing within 80% isodose decreased. In conclusion**,** this study investigated the effect of using contrast agents CT images on dose calculation. When CT number increased, percent difference of dose between plans with and without contrast agents increased. The correction method was developed to correct the CT number to density table and applied to contrast agents CT images. In final conclusion, the correction method worked well and can be applied in the clinic.

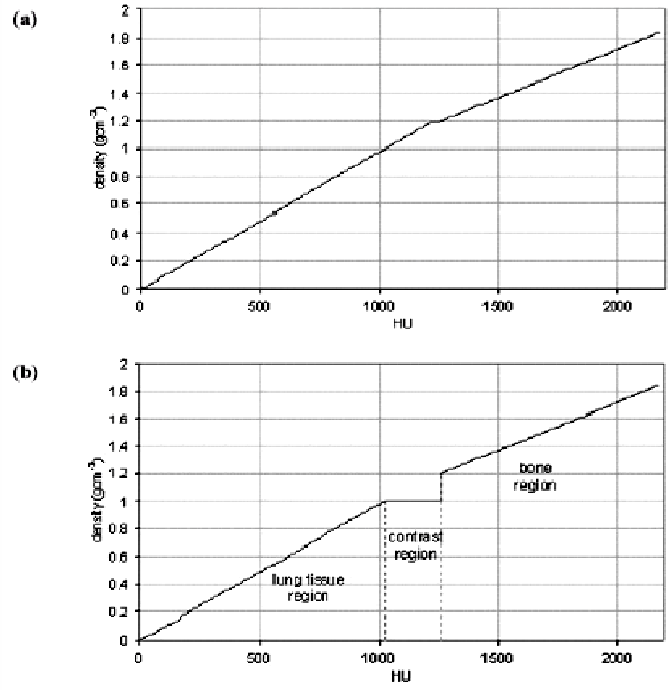


Figure 3.1 CT to density table that used in Burridge NA et al. 's study (a) original CT to density table (b) modified CT to density table, the density of 1 g/cm^3 to 1.2 g/cm^3 was changed to 1 g/cm^3.

Letourneau D et al. [11] studied the effect of CT contrast agents on IMRT dose calculation in head and neck cancer. Treatment planning system that used to perform treatment planning was Pinnacle^3 planning system (version 7.6, Phillips, Medison, WI), which used collapsed cone convolution superposition algorithm. Ten squamous cell carcinoma patients were studied. Sets of CT images were acquired on, one patient from PET CT (GE) and nine patients from CT scans (Siemens Biograph Duo PET-CT hybrid Scanner). All patients were administrated 60 mL intravenous contrast agents, 2 mL/seconds rate of injection and 25 seconds delay time. All images were transferred to treatment planning system. With contrast agents, tumor volume and organ at risks (soft tissue and vessel) were contoured from the CT images. Then dose of contrast agents CT images was calculated. Next, without contrast agents, the CT images without contrast were simulated by changing density within vessel to water density (1.00 g/cm^3 or 0 HU). The simulated CT images were used in order to eliminate error factors such as difference in source to skin distance that occurred in 2 sets of CT images (with and without CT contrast agents). In addition, the CT images

were still simulated with the density within to vessel to the cortical bone of 1.682 g/cm^3 or +1000 HU and air of 0.001 g/cm^3 or -1000 HU. Whole three plans used the same factor for planning which copied from an original plan before, then recalculated dose. CT contrast agents within carotid arteries and jugular vein induced shielding effect that influenced on dose distribution. Dose calculation for plan without contrast agents was more than that for plan with contrast agents and both plans had a little dose variation in organs at risks. When the density was changed within blood vessel to bone and air, dose variations at these regions increased. The most point dose variation for organs at risks occurred in blood vessel with air equivalent density. In conclusion, Intravenous contrast agents had no clinical effect significantly on IMRT dose calculation for head and neck cancer. Thus, it might be possible to use contrast agent CT images for IMRT treatment planning.

Nurushev T et al. [12] studied the effect of intravenous contrast agents on 3D conformal radiotherapy and IMRT for brain, thorax and abdomen regions. CT images of two sets (with and without contrast agents) were acquired and transferred to a treatment planning system. Enhanced CT images were administrated for 300 mgI/mL concentration with rate of injection 0.5 mL/secs for brain and 1 mL/secs for thorax and abdomen regions. First, without contrast agents CT images were used for dose calculation and then the parameters used for that plan were copied to with contrast agents CT images for dose calculation. They found that the effect of contrast agents depended on treatment anatomical regions, complexity of treatment plan and distance of beam through contrast agent region. The maximum dose difference for this study was 3%. Contrast agents can make the results over-estimated or under-estimated. There depended on ratio of contrast content within tumor volume versus the beam pathway. In conclusion, contrast agents have no clinical effect on fractionated radiotherapy.

Weber DC et al. [13] studied the effect of CT contrast agents filled in the bladder on a dose calculation in a prostate cancer. Treatment planning system that used to perform treatment planning was CadPlan 3.1.3, VARIAN® for 3-dimensional radiotherapy. They studied in five prostate cancer patients which have the most of the bladder opacification. During CT simulation contrast agents were injected to fill in the bladder. Then bladder opacification was computed by the mean of Hounsfield Unit

multiplied by third root of bladder volume (mean HU × [volume] $^{0.33}$). After bladder was filled with contrast agents then administrated IV contrast agents (omnipaque®, Scherring) of 30 cm^3 volume, and then pelvis started scanning. CT images were reconstructed and transferred to treatment planning system. Clinical target volume that included CTV, prostate, and seminal vesicle and organs at risk (bladder, rectum and femoral head) were contoured. Treatment planning was performed in with bladder contrast (bladder opacification) of 74 Gys prescribed dose, coplanar 6-fields technique for x-ray energy of 18 MV and doses were calculated, then overridden density within bladder to water density in order to simulate without bladder contrast. Plan with bladder contrast was copied to without bladder contrast for the purpose of controlling the related factors to be the same. Two plans were assessed by dose volume histograms for prostate and rectum, comparison of dose distributions and compensation of increase the monitor unit for the case of with bladder contrast. In conclusions, bladder contrast agents during CT simulation for prostate cancer have no clinical effect on dose distribution for prostate and rectum for 3-D conformal radiotherapy, with 18 MV x-ray and coplanar 6-fields technique.

Shibamoto Y et al. [14] studied a prospective study in the effect of CT contrast agents on dose calculation in 3D treatment planning at various anatomical regions. Treatment planning system that used to perform treatment planning was Eclipse Version 7.5.14.3 (Varian Medical System, Palo Alto, CA, USA) with pencil beam convolution algorithms for 3-dimensional radiotherapy. They studied in 26 cancer patients that excluded patients who weight over 65 kg. Patients were classified as the following; 5 patients of brain, 5 patients of neck, 5 patients of mediastinum, 5 patients of whole pevis and 6 patients of upper abdomen. Each patient was scanned for 2 sets of CT images both with and without contrast agents by multislice CT scanner (Phillip MX-8000). For with CT contrast, Iopamidol 100 mL (2mL/kg for or 100 mL for overweight 50 kg), 300 mgI/mL concentrations, rate of injection 1.5 mL/seconds for brain and 2 mL/seconds for other regions were administered. The delay time after administered, before scanning was 120 seconds for brain, 90 seconds for pelvis and 60 seconds for head and neck and upper abdomen. The variation in CT number in blood vessel and soft tissue are as the following; paraventricular deep white matter and transverse sinus for brain, sternocleidomastoid muscle and internal jugular vein for

head and neck, suprasupinatus muscle and superior vena cava for mediastinum, liver parenchyma and inferior vena cava for upper abdomen, and quadratus femoris muscle and common iliac vein for pelvis. Then, mean CT number and standard deviation were computed. First treatment planning was performed in with contrast agents, 4 MV for neck and 10 MV for other regions, and doses were assessed at isocenter for all patients. Then plan were copied to without contrast agents CT images set and monitor units were calculated. The maximum of mean of increase MU detected in conformal irradiation of liver cancer patient which radiation beam passed through liver, kidneys, spleen and vessel in patient's body, because these organs had large regions that filled with contrast agents. In conclusion, using CT contrast agents, did not affect significantly on dose calculation for radiotherapy treatment planning in brain, head and neck, mediastinum and pelvis, but affect on dose calculation for upper abdomen especially the beams passing through liver, spleen or kidney. Therefore in the upper abdomen, without contrast agents CT images were recommended for dose calculation in radiotherapy treatment planning.

CHAPTER IV
MATERIALS AND MEDTHODS

Retrospective study was used in this study. CT images and treatment plans of the cancer patients were obtained from the patient's medical record at Radiation Oncology Department, Faculty of medicine, Ramathibodi Hospital between January 2008 to January 2009.

4.1 Materials

4.1.1 Treatment planning system

The Pinnacle$^{3®}$ RTPS, version 7.6C was used for all dose calculation in this study as shown in Figure 4.1. The Pinnacle$^{3®}$ RTPS consists of Sun UNIX workstation and running by the Solaris operating system. The Pinnacle system provides an inclusive set of tools for set up and evaluate treatment plans. The software includes option for photon and electron beams treatment planning. The CT images data can be transferred from CT simulator workstation to treatment planning system. Algorithm used in Pinnacle is convolution-superposition algorithm to compute dose distributions and take the effects of beam modifiers, the source to skin distance, and tissue heterogeneities correction by convert CT number to mass density (gram per cm^3).

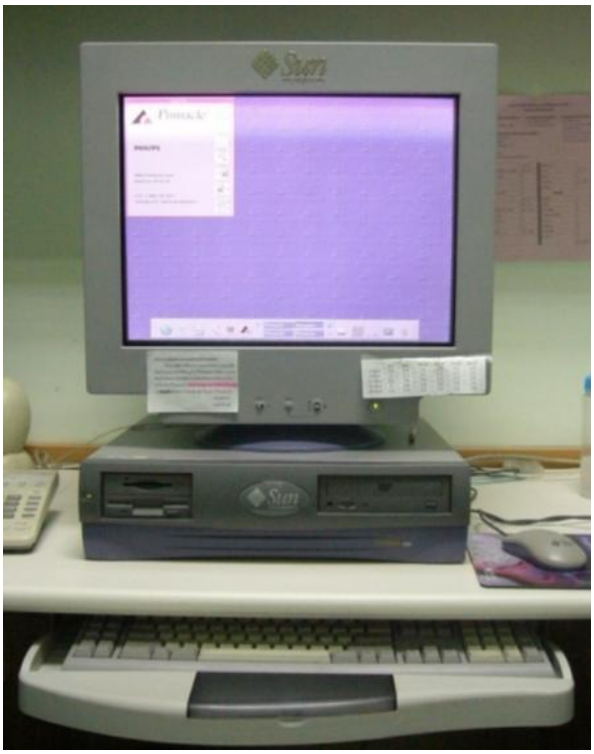


Figure 4.1 Treatment planning system – Pinnacle$^{3®}$, version 7.6C of Ramathibodi Hospital.

4.1.2 CT images

Scopes of this study was studied for cancer patients in brain, thorax and upper abdomen regions in Radiation Oncology department, Ramathibodi Hospital with treatment planning technique using 3D-CRT and simulation using CT simulator data from January 2008 to January 2009. The planning CTs were done on Philips, MX 8000 IDT (Figure 4.2). In this study, the selected patients were scanned for both with and without contrast agents CT image sets.

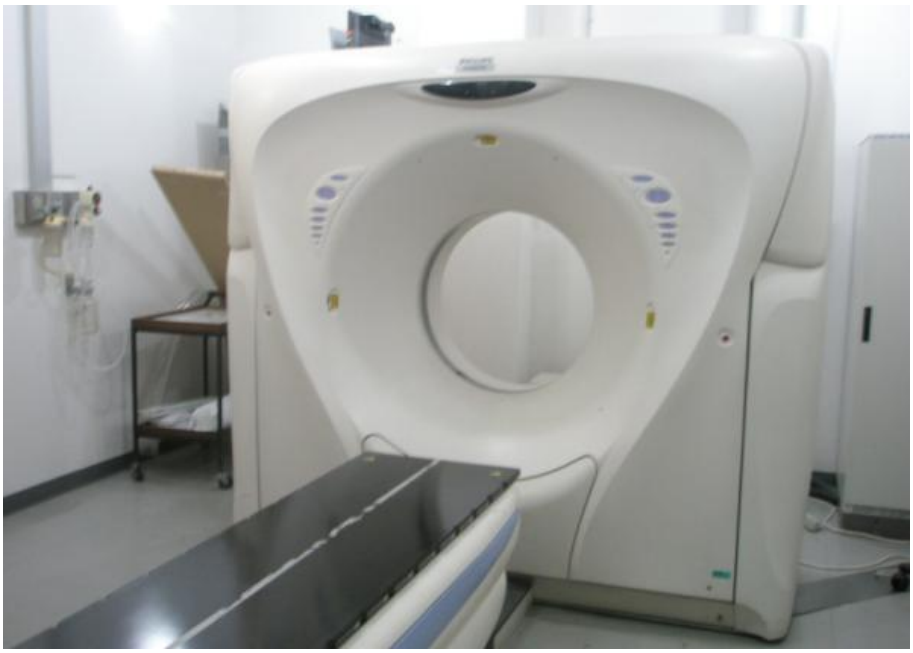


Figure 4.2 CT simulator, Philip, Mx 8000 IDT in radiotherapy department at Ramathibodi hospital.

4.1.2.1 Brain region

The CT scan was performed in helical mode, 120 kVp, 350 mAs and 3.0 mm slice thickness for both with and without contrast agent CT images.

For the CT images with contrast agent, all patients were administrated 50 ml of contrast agents (Ultravist 300 mgI/ml) with 2.5 ml / seconds rate of injection. Scanning began for 25 seconds after the CT number at ascending aorta were 150 HU.

4.1.2.2 Thorax region

The CT scan was performed in helical mode, 140 kVp, 250 mAs and 5.0 mm slice thickness for both with and without contrast agent CT images.

For the CT images with contrast agent, all patients were administrated 100 ml of contrast agents (Ultravist 300 mgI/ml) with 2.5 ml / seconds rate of injection. Scanning began for 25 seconds after the CT number at ascending aorta were 150 HU.

4.1.2.3 Upper abdomen region

The CT scan was performed in helical mode, 140 kVp, 250 mAs and 5.0 mm slice thickness for both with and without contrast agent CT images.

For the CT images with contrast agent, all patients were administrated 100 ml of contrast agents (Ultravist 300 mgI/ml) with 2.5 ml / seconds rate of injection. Scanning began for 45 seconds after the CT number at ascending aorta were 150 HU.

4.1.3 Treatment plans

Treatment plans of each selected cancer patients for brain, upper abdomen and thorax regions used in this study were approved by radiation oncologists and these treatment plans were already used in clinical treatments. So in this study, these treatment plans will be called "approved treatment plan". The treatment planning techniques in each brain, thorax and upper abdomen regions are shown in Table 4.1, 4.2 and 4.3, respectively.

Table 4.1 Treatment planning techniques for brain cancer patients.

Case	*Disease*	*Beam Direction*	*Energy*	*Prescribed dose at isocenter (*Gy)
1	Oligodendroglioma	AP, Lt lat, Rt lat	6 MV	59.4
2	Astrocytoma	AP, PA, Rt lat, RAO, LPO	6 MV, 10 MV	60.4
3	Brain Cancer	Rt lat, Lt lat	6 MV	81.7
4	Oligodendroglioma	AP, PA, Rt lat, Lt lat, RAO, RPO	6 MV, 10 MV	59.4
5	Glioblastoma Multiforme	PA, Rt lat, Lt lat, Rt lat w15, Lt lat w15	6 MV	54

Table 4.2 Treatment planning techniques for thorax cancer patients.

Case	*Disease*	*Beam Direction*	*Energy*	*Prescribed dose at isocenter (*Gy)
1	Thymoma	AP, PA	10 MV	50
2	Mucoepidermoid	AP, PA	6 MV, 10 MV	50
3	Lung Cancer	AP, PA	6 MV, 10 MV	39
4	Esophageal Cancer	AP, PA, RPO, LAO	6 MV	59.4
5	Lung Cancer	AP, PA, LAO, RPO	6 MV, 10 MV	54
6	Esophageal Cancer	AP, PA, Rt lat, Lt lat	10 MV	54

Table 4.3 Treatment planning techniques for the upper abdomen cancer patients.

Case	*Disease*	*Beam Direction*	*Energy*	*Prescribed dose at isocenter (*Gy)
1	Cholangioma	AP, PA, RAO, LPO	10 MV	39.6
2	Pancreatic Cancer	AP, PA, Rt lat, Lt lat	10 MV	60
3	Lymphoma	AP, PA, RPO, Lt lat	10 MV	36
4	Stomach Cancer	AP, PA, Rt lat, Lt lat	10 MV	39.6

4.2 Methods

4.2.1 Brain region

4.2.1.1 Five patients were selected as shown in Table 4.1. The CT images were transferred from CT simulator work station to the treatment planning system.

4.2.1.2 Planning for “without contrast agent CT images”

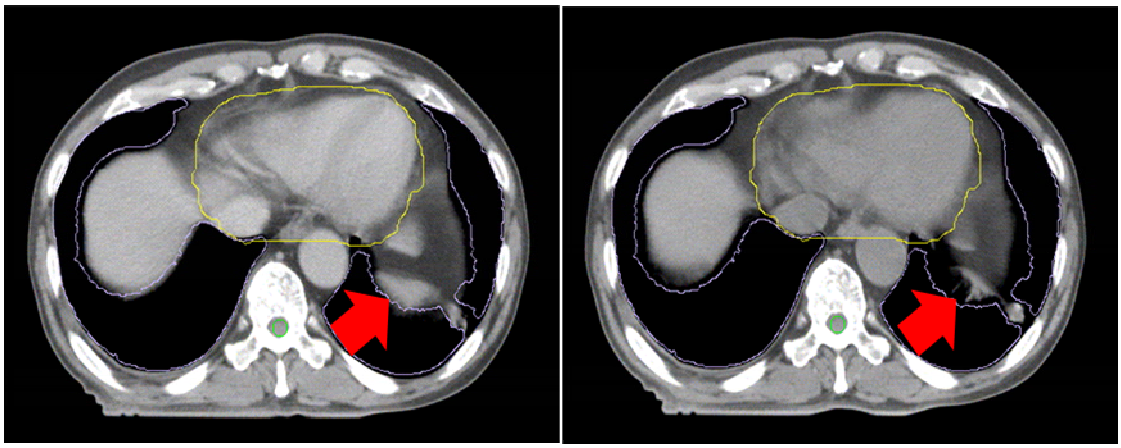
In each patient, the first treatment plan was performed with the images in without contrast agent by copying the parameters from approved treatment plan as shown in Table 4.1 that used in patient treatment to without contrast agent plan. After that, radiation dose was calculated again from the without contrast agents CT images. The Monitor Units (MUs) were recorded for each radiation beam.

4.2.1.3 Planning for “with contrast agent CT images”

In the second step, the parameters from the first plan were copied to with contrast agent CT images. The same MUs of individual beams from the first plan were copied to the second plan and then the dose was calculated from with contrast agent CT images.

4.2.2 Thorax region

4.2.2.1 Six patients were selected as shown in Table 4.2. The CT images were transferred from CT simulator work station to radiotherapy treatment planning system.



(a) (b)

Figure 4.3 (a) “with contrast agent CT images” fused with the “without contrast agent CT images" (b) at the same slice number.

Figure 4.3 shows the CT images at the same slice number, with contrast agent (a) and without contrast agent (b) with the red arrow pointed at the example difference of two CT images caused by patient respiration. In order to reduce uncertainty due to respiration and cardiac motion, one of CT image set was simulated.

In this study, without contrast agent of thorax and upper abdomen CT images was imitated by overriding the density to the organs or regions using the density obtained from the original CT images without contrast agent. Because, overriding the density from with contrast agent CT images to without contrast agent CT images was easier than another method.

4.2.2.2 Overriding of CT images with contrast agent by using CT number of non contrast images, as the following steps.

i. With contrast agent CT images, the regions that filled with contrast agent such as heart and great vessel in thorax regions were delineated.

ii. The mean CT number of the organs in section (i.) of non contrast images were estimated and used for the contrast images by overriding tool. Then images were called “overriding density CT images” as shown in Figure 4.4.

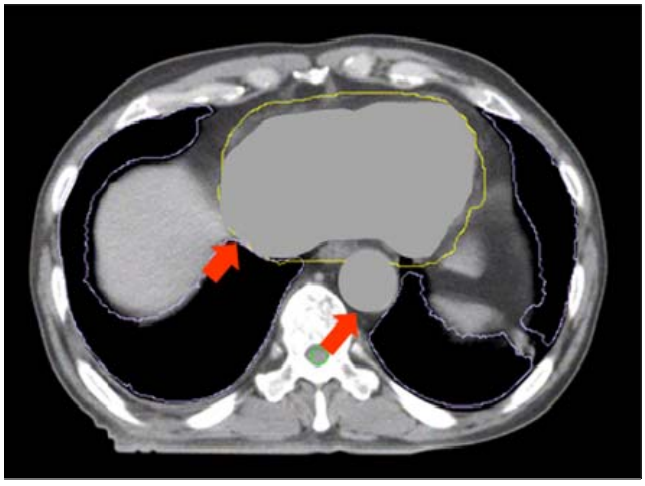


Figure 4.4 Overriding density CT images for thorax region.

4.2.2.3 The treatment plans shown in Table 4.2 were performed using overriding density CT images. Then the doses were calculated from the overriding density CT images. The MUs were recorded for each radiation beam.

4.2.2.4 The plans in section 4.2.2.3 were copied and pasted in the CT images with contrast agent. The same MUs for each beam were used to calculate the doses.

4.2.3. Upper abdomen region

4.2.3.1 Five patients were selected as shown in Table 4.2. These CT images were transferred from CT simulator work station to radiotherapy treatment planning system.

4.2.3.2 Like the thorax region, overriding of CT images with contrast agent by using CT number of non contrast images, as the following steps.

i. With contrast agent CT images, the regions that filled with contrast agent namely liver, spleen kidneys and vessels were delineated.

ii. The mean CT number of the organs in section (i.) of non contrast images were estimated and used for the contrast images by overriding tool. Then images were called “overriding density CT images” as shown in Figure 4.5.

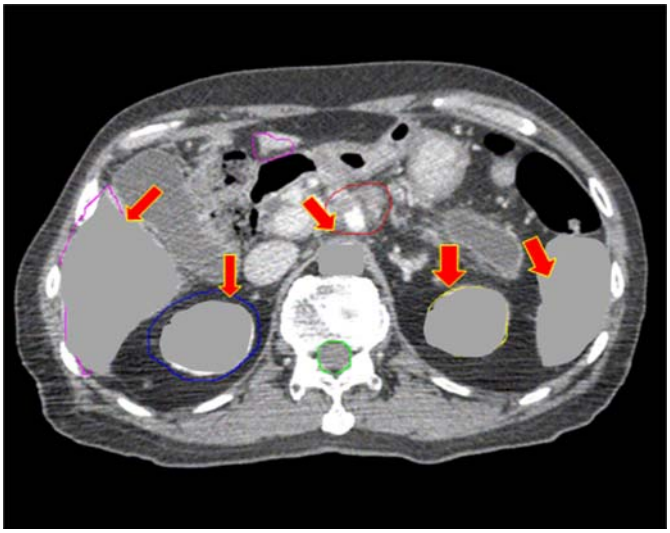


Figure 4.5 Overriding density CT images for upper abdomen region.

4.2.3.3 The treatment plans shown in Table 4.3 were performed using overriding density CT images. Then the doses were calculated from the overriding density CT images. The MUs were recorded for each radiation beam.

4.2.3.4 The plans in section 4.2.3.3 were copied and pasted in the CT images with contrast agent. The same MUs for each beam were used to calculate the doses.

4.2.4. Results analysis

The results comparison of contrast agent and non contrast agent plans were evaluated by two methods, mean dose and fluence map.

4.2.4.1 Mean dose

Mean dose from dose volume histogram of tumor volume and organs at risk were recorded. The prescribed dose was normalized for each patient to 100% and normalized dose for tumor volume and organs at risk were defined by dividing mean dose by prescribed dose and multiplied by 100% as shown in Equation (4).

$$D_{normalize} = \frac{D_{mean}}{D_{prescribe}} \times 100\% \qquad \text{.....(4)}$$

where $D_{normalize}$ is normalized dose

D_{mean} is mean dose from dose volume histogram

$D_{prescribe}$ is prescribed dose

Then the mean dose was compared by calculating the percentage of dose difference as shown in Equation (5).

$$\%dose\ different = \left(\frac{D_{with} - D_{without}}{D_{without}} \right) \times 100\%, \qquad \text{.....(5)}$$

where D_{with} is mean dose from with contrast agents plan

$D_{without}$ is mean dose from without contrast agents plan

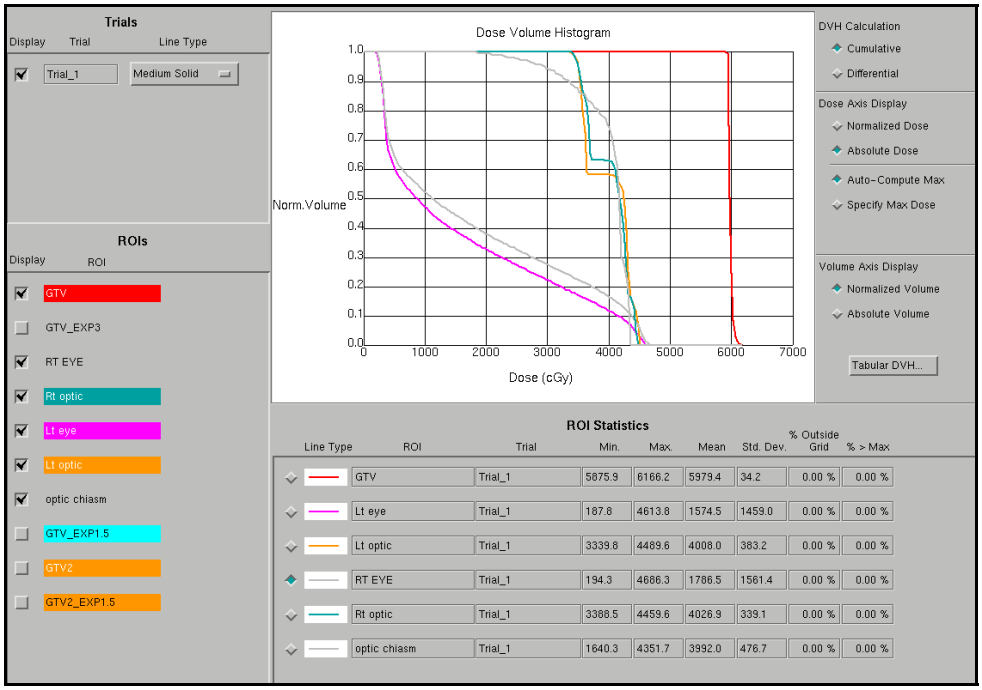


Figure 4.6 Dose Volume Histogram window from The Pinnacle TPS version 7.6C.

4.2.4.2 Planar dose map (Fluence map)

The planar images were acquired for each beam separately. The planar dose map was computed for each field at 100 cm SPD (Source to Plane Distance) of patient with 1 mm resolution [15]. Each beam's fluence map of both groups was computed by using the OmniPro-I′mRT software version 1.6 with gamma evaluation as shown in Appendix A. The gamma evaluation, with criteria of 3% of maximum dose difference and 3 mm distance to agreement shown in the Appendix B was applied to generate the gamma map. The OmniPro I′mRT software was used to compared the planar dose of with and without contrast agents by using the criteria as shown in Appendix C that the percentage of pixel with gamma value more than 1 must be ≥ 95% and mean gamma value must be more than 0.5.

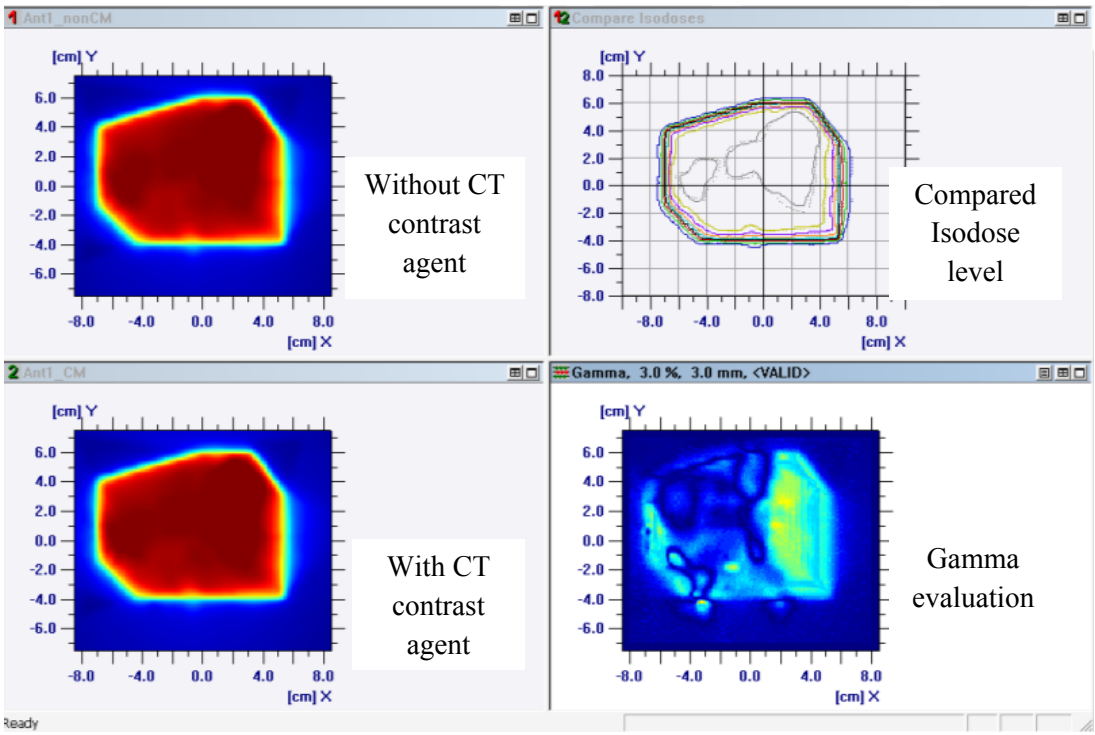


Figure 4.7 Verification of dose distributions calculated by Pinnacle TPS, compared between with and without CT contrasts agents in the OmniPro I′mRT software.

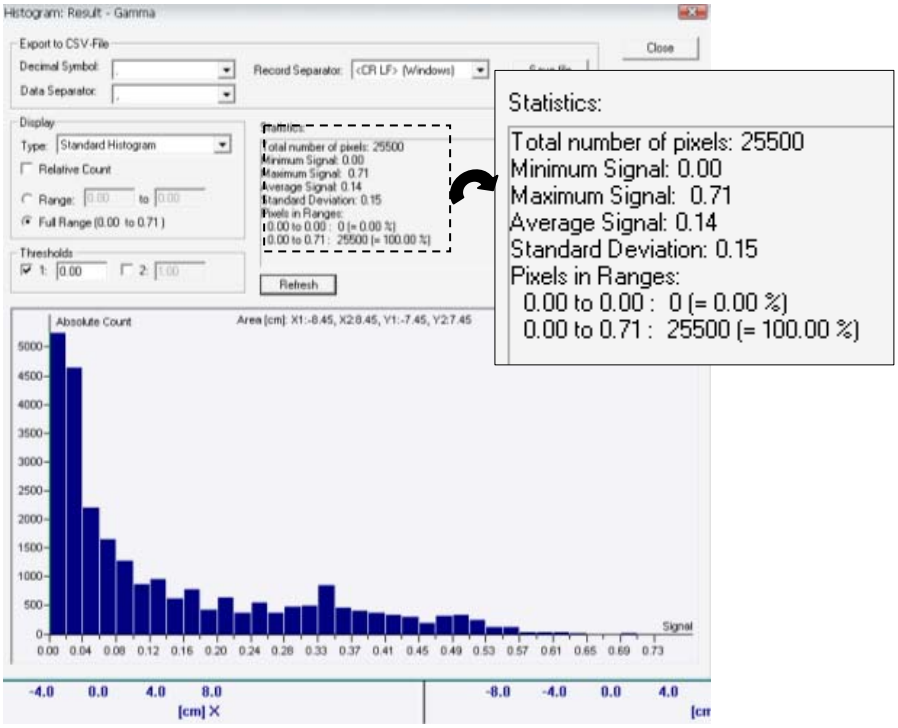


Figure 4.8 Gamma result in the OmniPro I′mRT software.

4.2.4 Statistical analysis

The mean and standard deviation (SD) were presented by descriptive statistics. The paired sample t-test (α=0.05) was used to analyze the two data sets statistically.

CHAPTER V
RESULTS AND DISCUSSION

5.1 Comparison of mean dose

Mean doses of tumor volume and organs at risk for each patient from dose volume histogram were recorded for both plans; with and without contrast agent CT images. Mean doses of two plans were normalized with the prescribed dose (Equation 4), and then compared by using statistical analysis. The mean of the normalized dose were averaged from the values of number of patients and the percentage of dose difference were calculated from Equation (5) as illustrated in Table 5.1, 5.2 and 5.3 for brain, thorax and upper abdomen regions, respectively.

Table 5.1 Comparison of the dose normalized with the prescribed dose of the two imaged groups using the percentage of dose difference and the paired sample t-test for brain region (n=5).

	Mean normalized dose ± SD (%)		**% dose difference**	**p- value**
	Without contrast	With contrast		
Tumor volume	102.07±3.07	102.07±3-06	0.00	0.8033
Left eye	12.66±11.60	12.64±11.58	-0.16	0.3046
Left optic	31.97±34.60	31.93±34.53	-0.13	0.3399
Right eye	19.44±16.62	19.44±16.61	0.00	0.6657
Right optic	26.75±27.61	26.75±27.59	0.00	0.7040
Optic chiasm	60±35.62	59.97±35.61	-0.05	0.3046
Brain stem (n=4)	43.68±41.03	43.69±41.05	0.02	0.2522

From Table 5.1, the percentage of dose difference including p-value in the bracket for tumor volume, left eye, left optic, right eye, right optic, optic chiasm and brain stem are 0% (0.8033),-0.06% (0.3046),-0.13 (0.3399), 0% (0.6657), 0% (0.7040),-0.05% (0.3046) and 0.02% (0.2522), respectively. All of the results show no significant difference between the two plans.

Table 5.2 Comparison of the dose normalized with the prescribed dose of the two imaged groups using the percentage of dose difference and the paired sample t-test for thorax region (n=6).

	Mean normalized dose ± SD (%)		**% dose difference**	**p- value**
	overriding density	non-overriding density		
Tumor volume	103.14±4.75	102.44±3.97	-0.68	0.1015
Spinal cord	36.71±5.2	36.47±5.37	-0.65	0.0835
Left lung	17.93±8.21	17.87±8.18	-0.33	0.0771
Right lung	46.15±22.22	45.94±22.03	-0.46	0.2875
Heart (n=5)	42.92±16.53	42.59±16.65	-0.77	0.0366

From Table 5.2, the percentage of dose difference including p-value in the bracket for tumor volume, spinal cord, left lung, right lung and heart are -0.68% (0.1015), -0.65% (0.0835), -0.33% (0.0771) , -0.46% (0.2875) and -0.77% (0.0366), respectively. These results show no significant difference between non-overriding density and overriding density CT images treatment plan for tumor volume, spinal cord, left lung and right lung except the heart. However, the difference was very small (-0.77%). The reasons of the significant difference are because the CT images of the heart have a lot of contrast agent with high concentration and large region.

Table 5.3 Comparison of the dose normalized with the prescribed dose of the two imaged groups using the percentage of dose difference and the paired sample t-test for upper abdomen region (n=4).

	Mean normalized dose ± SD (%)		**% dose difference**	**p- value**
	overriding density	non-overriding density		
Tumor volume	99.96±0.44	99.62±0.36	-0.34	0.1323
Spinal cord	44.98±30.25	44.98±30.18	0.00	0.2062
Liver	24.41±30.27	24.23±30.01	-0.74	0.2602
Spleen	17.84±11.26	17.75±11.20	-0.50	0.0742
Right kidney	19.7±30.93	19.6±30.8	-0.51	0.2465

From Table 5.3, the percentage of dose difference including p-value in the bracket for tumor volume, spinal cord, liver, spleen and right kidney are -0.34% (0.1323), 0% (0.2062), -0.74% (0.2062), -0.50% (0.0742) and -0.51% (0.2465), respectively. Again, all of the results show no significant difference between non-overriding density and overriding density CT images treatment plan.

5.2 Gamma evaluation

The results of gamma evaluation from the comparison between two planar dose maps, which obtained from treatment plans of with and without contrast agent CT images for brain, thorax and upper abdomen, are shown in Table 5.4, 5.5 and 5.6 respectively, in the tables showing the beam direction of each planar dose map, number of pixel (pixel size = 1 mm^2, depended on size of field size), average gamma value, SD of gamma value and percent pixel pass are shown. Acceptable criteria for evaluation are that the average gamma value is less than 0.5 and the percentage of pixel pass is more than 95% (Appendix C).

Table 5.4 Individual beam results of gamma evaluation, average gamma value and percent pixel pass for brain region.

Case No.	Direction beam	No. of pixel	average gamma value	SD	%pixel pass	acceptable
1	Ant 2-2	8500	0.02	0.05	100%	Yes
	Ant2	8500	0.02	0.05	100%	Yes
	L lat 1-1s	18200	0.04	0.09	99.87%	Yes
	L lat 2-2	13000	0.02	0.06	99.92%	Yes
	L lat2	13000	0.02	0.06	99.92%	Yes
	L lat 1-2a	18200	0.03	0.09	99.87%	Yes
	R lat 1-2a	18200	0.04	0.09	99.89%	Yes
	R lat 2-2	13000	0.02	0.05	99.92%	Yes
	R lat 1-1s	18200	0.04	0.09	99.89%	Yes
	R lat2	13000	0.02	0.05	99.92%	Yes
2	AP	14400	0.04	0.09	100%	Yes
	Lt lat2	11000	0.12	0.22	98.75%	Yes
	Lt lat	15600	0.12	0.22	99.01%	Yes
	PA	14400	0.18	0.26	98.88%	Yes
	RAO	11000	0.06	0.11	100%	Yes
	RPO	12000	0.25	0.31	95.41%	Yes
	Rt lat	15600	0.12	0.22	98.98%	Yes
3	Lt frontal	15600	0.03	0.07	99.94%	Yes
	Lt lat	30000	0.03	0.09	99.86%	Yes
	Rt frontal	15600	0.03	0.08	99.90%	Yes
	Rt lat	30000	0.03	0.08	99.96%	Yes
4	AP	12650	0.05	0.08	99.85%	Yes
	LPO2	17050	0.03	0.06	99.87%	Yes
	LPO	17050	0.03	0.06	99.87%	Yes
	Lt lat	18700	0.04	0.07	99.84%	Yes
	Lt lat RF	14250	0.03	0.06	99.92%	Yes

Table 5.4 (continued) Individual beam results of gamma evaluation, average gamma value and percent pixel pass for brain region.

Case No.	Direction beam	No. of pixel	average gamma value	SD	%pixel pass	acceptable
4	PA	12650	0.03	0.08	99.78%	Yes
	RAO2	17050	0.06	0.10	99.88%	Yes
	RAO	17050	0.06	0.09	99.88%	Yes
	Rt inf RF	16500	0.04	0.10	99.78%	Yes
	Rt lat	18700	0.04	0.07	99.86%	Yes
5	Lt lat1	15000	0.01	0.02	100%	Yes
	Lt lat1 w15	15000	0.01	0.02	100%	Yes
	Lt lat2	10500	0.01	0.02	100%	Yes
	Post brain	15000	0.01	0.02	100%	Yes
	Rt lat1	15000	0.02	0.02	100%	Yes
	Rt lat2	10500	0.01	0.02	100%	Yes
	Rt lat w15	15000	0.02	0.02	100%	Yes

Table 5.5 Individual beam results of gamma evaluation, average gamma value and percent pixel pass for thorax region.

Case No.	Direction beam	No. of pixel	average gamma value	SD	%pixel pass	acceptable
1	Ant1	25500	0.14	0.15	100%	Yes
	Ant2	25500	0.14	0.15	100%	Yes
	Post1	25500	0.11	0.13	100%	Yes
	Post2	25500	0.07	0.15	100%	Yes
2	Ant	36000	0.11	0.11	100%	Yes
	Beam1	36000	0.07	0.09	100%	Yes
	Beam2	36000	0.02	0.03	100%	Yes
	Post	36000	0.03	0.05	100%	Yes

Table 5.5 (continued) Individual beam results of gamma evaluation, average gamma value and percent pixel pass for thorax region.

Case No.	Direction beam	No. of pixel	average gamma value	SD	%pixel pass	acceptable
3	Ant	20900	0.08	0.08	100%	Yes
	LAO2	15500	0.04	0.05	100%	Yes
	Post	20900	0.03	0.04	100%	Yes
	RAO2	15500	0.06	0.05	100%	Yes
4	1P	35200	0.06	0.11	100%	Yes
	1A	35200	0.2	0.16	100%	Yes
	2A	35200	0.17	0.15	100%	Yes
	2P	35200	0.07	0.12	100%	Yes
	3LAO	27300	0.14	0.13	100%	Yes
	3RPO	27300	0.07	0.07	100%	Yes
5	1Ant	21450	0.13	0.17	100%	Yes
	1Post	21450	0.05	0.07	100%	Yes
	2.1A 10x	24375	0.11	0.14	100%	Yes
	2.1P 10x	24375	0.04	0.06	100%	Yes
	2 post	24375	0.04	0.08	100%	Yes
	2 Ant 6x	24375	0.14	0.17	100%	Yes
	3A av cord	18525	0.09	0.11	100%	Yes
	3P av cord	18525	0.03	0.06	100%	Yes
	4A GTV	8400	0.11	0.11	100%	Yes
	4P GTV	8400	0.08	0.07	100%	Yes
6	Ant1	39200	0.13	0.15	100%	Yes
	Ant2	32200	0.14	0.17	100%	Yes
	Lt lat3	16200	0.07	0.09	100%	Yes
	Post1	39200	0.03	0.06	100%	Yes
	Post2	32200	0.03	0.06	100%	Yes
	Rt lat3	16200	0.05	0.06	100%	Yes

Table 5.6 Individual beam results of gamma evaluation, average gamma value and percent pixel pass for upper abdomen region.

Case No.	Direction beam	No. of pixel	average gamma value	SD	%pixel pass	acceptable
1	Ant	46000	0.07	0.07	100%	Yes
	Post	46000	0.03	0.03	100%	Yes
	Lt lat	31500	0.10	0.11	100%	Yes
	RPO	35700	0.11	0.10	100%	Yes
2	Ant2	19200	0.04	0.08	100%	Yes
	Ant1	19200	0.04	0.07	100%	Yes
	Lt abd	16800	0.04	0.08	100%	Yes
	Post 1	19200	0.05	0.07	100%	Yes
	Rt abd	16800	0.19	0.19	100%	Yes
3	Ant abd2	9000	0.06	0.06	100%	Yes
	Ant abd	9000	0.06	0.06	100%	Yes
	LPO	9900	0.09	0.11	100%	Yes
	Post abd	9000	0.06	0.07	100%	Yes
	RAO	9900	0.07	0.11	100%	Yes
4	Ant abd2	19500	0.05	0.05	100%	Yes
	Ant abd1-1	38250	0.12	0.10	100%	Yes
	Ant abd	38250	0.12	0.10	100%	Yes
	Lt lat	13650	0.05	0.06	100%	Yes
	Post abd 1-1	38250	0.07	0.11	100%	Yes
	Post abd	38250	0.10	0.11	100%	Yes
	Rt lat 2	13650	0.09	0.10	100%	Yes

From Table 5.4, the results of gamma evaluation for brain region are shown. All planar dose comparisons have the average gamma value less than 0.5 and all of them have the percentage of pixel pass with more than 95%. Therefore all planar doses of two treatment plans (with and without CT contrast agents) show no difference in the dose distributions.

From Table 5.5 and 5.6, the results of gamma evaluation for thorax and upper abdomen regions are shown. Also, all planar dose comparisons have the average gamma value with less than 0.5 and the percentage of pixel pass with 100% (pass the criteria of percentage of pixel pass more than 95%). Again all planar doses of two plans (non-overriding density and overriding density CT images) have no difference in the dose distributions.

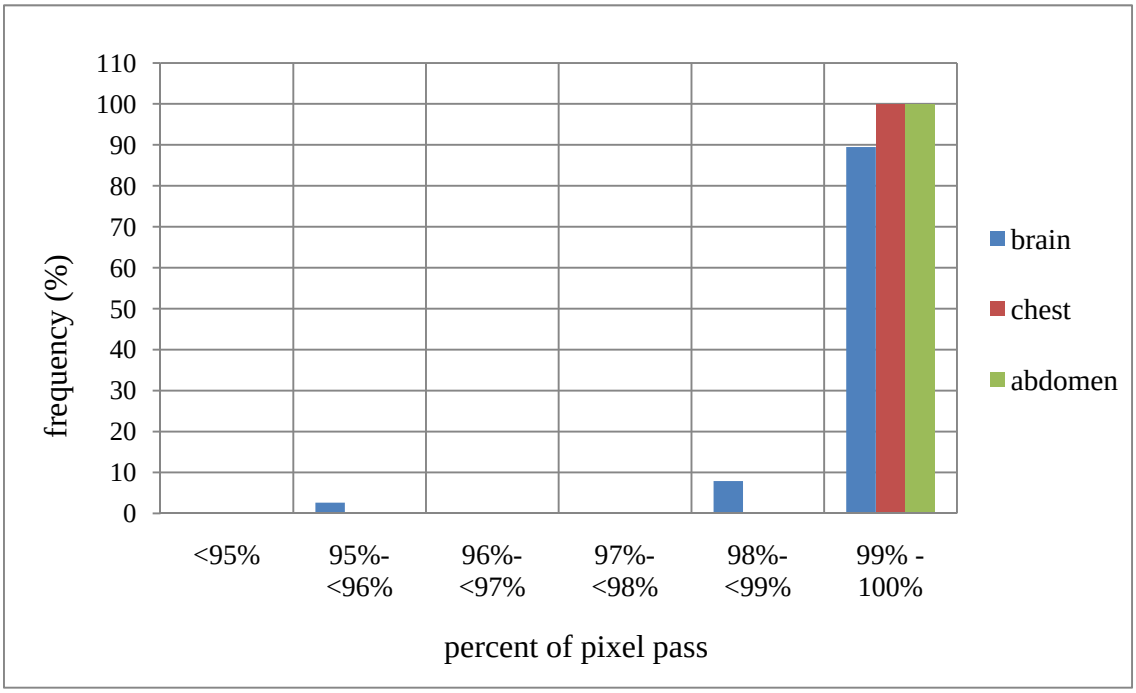


Figure 5.1 Histograms of the summary for the distributions of the percentage of pixel pass for brain, thorax, and upper abdomen regions.

The histogram in Figure 5.1 show the summary results for brain, thorax, and upper abdomen regions. All of three parts of cancer patients show good results. All planes present the percentage of pixel pass with more than 95%. In brain region, the results of the comparison show poorest when compared with other regions, because the original of CT images were used for brain in without contrast agent while others used the simulated one. The advantage of using overriding density CT images is to eliminate the confounding factor such as patient deformation and source to skin distance variation, so the thorax and upper abdomen regions give better results than the brain region.

The results from two methods are comparable. There is no difference between treatment plans of with and without CT contrast agent.

Normally the delineation is performed to do on “with contrast agent CT images” by then fusion with “without contrast agent CT images”. However from this study, there is no difference in dose calculation between with and without contrast agent CT images, so the delineation and dose calculation can be done on the with contrast agent CT images. Nevertheless Shibamoto et al [14]’s study showed the difference between with and without contrast agent plan at upper abdomen region (dose difference over 2%). Because the overridden density technique was not implemented in their study, so two CT image sets were different in SSD or patient deformation which leads to disagreement results with our results.

The results of mean dose comparison show the dose difference between with and without contrast agent CT images less than 1%. So, if the criteria of 1%/ 1 mm in gamma evaluation are used, the results maybe pass the criteria of percentage of pixel pass more than 95%.

Table 5.7 shows the results of gamma evaluation from criteria of 1% /1 mm and 3%/ 3 mm for brain region. As a result, the criteria of 1% 1 mm shows the percentage of pixel pass with more than 95% except case number 2 shows the poorest results especially in beam direction of Lt lateral, PA and RPO, the percentage of pixel pass with less than 95% is failed. The reason is that the position error might be more pronounced between two phases (with and without contrast agent) of CT images.

Table 5.7 Individual beam results of gamma evaluation, compared between criteria of 1% 1 mm and 3% 3 mm for brain region.

Case No.	**Direction beam**	**%pixel pass**	
		1%1mm	**3%3mm**
1	Ant 2-2	99.48%	100%
	Ant2	99.51%	100%
	L lat 1-1s	98.40%	99.87%
	L lat 2-2	99.45%	99.92%

Table 5.7 (continued) Individual beam results of gamma evaluation, compared between criteria of 1% 1mm and 3% 3mm for brain region.

Case No.	Direction beam	%pixel pass	
		1%1mm	3%3mm
1	L lat2	99.45%	99.92%
	L lat 1-2a	98.55%	99.87%
	R lat 1-2a	97.95%	99.89%
	R lat 2-2	99.72%	99.92%
	R lat 1-1s	97.75%	99.89%
	R lat2	99.72%	99.92%
2	AP	97.97%	100%
	Lt lat2	87.04%	98.75%
	Lt lat	84.80%	99.01%
	PA	79.20%	98.88%
	RAO	95.30%	100%
	RPO	69.19%	95.41%
	Rt lat	86.62%	98.98%
3	Lt frontal	99.02%	99.94%
	Lt lat	98.87%	99.86%
	Rt frontal	98.59%	99.90%
	Rt lat	98.40%	99.96%
4	AP	98.79%	99.85%
	LPO2	99.41%	99.87%
	LPO	99.41%	99.87%
	Lt lat	99.22%	99.84%
	Lt lat RF	99.44%	99.92%
	PA	98.96%	99.78%
	RAO2	97.20%	99.88%
	RAO	97.63%	99.88%
	Rt inf RF	98.01%	99.78%

Table 5.7 (continued) Individual beam results of gamma evaluation, compared between criteria of 1% 1mm and 3% 3mm for brain region.

Case No.	**Direction beam**	**%pixel pass**	
		1%1mm	**3%3mm**
4	Rt lat	99.26%	99.86%
5	Lt lat1	100%	100%
	Lt lat1 w15	100%	100%
	Lt lat2	100%	100%
	Post brain	100%	100%
	Rt lat1	100%	100%
	Rt lat2	100%	100%
	Rt lat w15	100%	100%

CHAPTER VI
CONCLUSIONS

The dose calculation in 3-Dimensional Conformal Radiotherapy (3D-CRT) was compared for brain, thorax and upper abdomen regions by comparison between treatment plans of “with and without contrast agent CT images”. The dose difference was analyzed using paired sample t-test and dose distribution was analyzed using gamma evaluation with the criteria 3% of maximum dose difference and 3 mm distance to agreement, the conclusions can be drawn as the followings:

1. Mean dose between with and without contrast agent plans are not significant difference (p-value > 0.05) for brain, thorax and upper abdomen regions at tumor volume and organs at risk. However the heart organ in the thorax region shows more dose difference among others but its difference still less than 1%.

2. Gamma evaluation results showed no significant difference between with and without CT contrast agent plans (the percentage of pixel pass more than 95% and mean gamma value less than 0.5).

From two evaluation tool results, using of CT contrast agent for brain, thorax, and upper abdomen regions at the time of CT simulation dose not significantly affect dose calculation in three dimensional conformal radiotherapy techniques at Ramathibodi Hospital. Even though criteria of 1%/1mm was used for only brain region the results still showed no difference except for case number 2 which might be position error between two sets of CT images. Nevertheless the somewhat dose difference in the heart volume for thorax region was found, but the advantage of using contrast agent are more useful than not using it. This can be compromised between clearer lesion and less accurate dose calculation but saving more time to perform an effective 3D treatment planning dose calculation.

Since contrast agent does not significantly affect dose calculation especially for thorax and upper abdomen regions which have the most amount of contrast agent concentration, largest area, and highest density of CT contrast agent so there could be implied that in other regions, the contrast agent dose not significantly affect dose calculation too. Above all, the contrast agent dose not significantly affect the dose calculation at any regions for 3D conformal radiotherapy technique with Pinnacle Treatment Planning version 7.6C at Ramathibodi Hospital.

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APPENDICES

APPENDIX A

Gamma evaluation [16, 17]

The gamma evaluation is a measurement of disagreement of two dose distributions such as calculate and measure dose distribution. Using the simplest methods, e.g. comparing isodoses (distance to agreement (DTA); the DTA is the distance between a dose point in the first distribution and the nearest point in the second distribution containing the same dose value) or dose difference for compare two dose distribution may not be appropriate because the misjudgment when compare two dose distributions may occur in the following cases:

i. The difference between two dose-distributions can be large in high dose gradient regions, even if the isodoses are relatively close to each other.

ii. The DTA between two dose distributions can be large in regions with a flat dose distribution, although the difference in dose may be quite small.

The gamma method combines both methods mentioned above (dose-difference and distance-to-agreement (DTA)).

For analysis can define dose difference and DTA pass/fail criteria, if both parameters (dose and DTA) are outside their pass/fail criteria, the agreement "fails" according to the gamma method (gamma value > 1) or if only one parameter is outside the defined pass/fail criteria but the other well inside, the result of the comparison can still pass the calculation (gamma value <1).

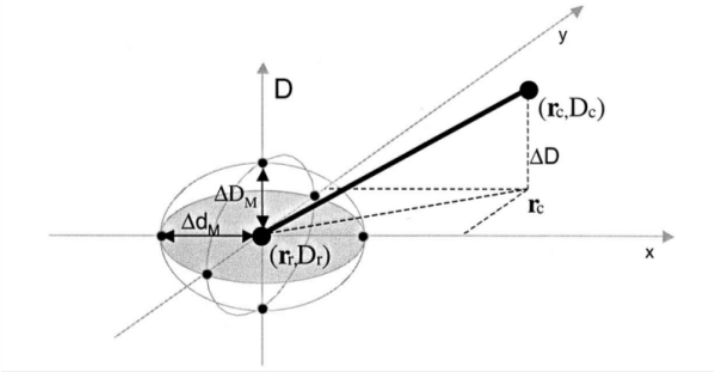

Figure 1a Schematic representation of the concept of gamma method

In Figure 1a the reference and compared dose are denoted by $D_r(r)$ and $D_c(r)$, acceptance criteria for dose difference and distance to agreement are denoted by ΔD_M and Δd_M. The point position (r_r, D_r) represent to reference point at position r_r, receiving dose D_r and (r_c, D_c) represent to compared point at position r_c, receiving dose D_c

The surface representing the acceptance criteria is an ellipsoid defined by

$$1 = \sqrt{\frac{\Delta r^2}{\Delta d_M^2} + \frac{\Delta D^2}{\Delta D_M^2}} \qquad \text{……(5)}$$

Where, $\Delta r = |r_r - r_c|$ is the distance between the reference and compared point and $\Delta D = D_c(r_c) - D_r(r_r)$ is the dose difference at position r_c relative to the reference dose D_r in r_r.

The gamma value for the compared point r_c is defined as

$$\gamma(r_c) = min\{\ \Gamma(r_c, D_c)\ \} \ \forall\ \{\ r_r\ \} \qquad \text{…….(6)}$$

Where,

$$\Gamma_r(r_c, D_c) \equiv \sqrt{\frac{\Delta r^2}{\Delta d_M^2} + \frac{\Delta D^2}{\Delta D_M^2}} \qquad \text{……..(7)}$$

For compared distribution to match the reference dose in r_r it needs to contain at least one point (r_c, D_c) lying within the ellipsoid of acceptance

$$\Gamma_r(r_c, D_c) \equiv \sqrt{\frac{\Delta r^2}{\Delta d_M^2} + \frac{\Delta D^2}{\Delta D_M^2}} \le 1 \qquad \text{…….(8)}$$

Thus, the pass-fail criteria are:

$\gamma(r_c) \le 1$ is mean compared passes

$\gamma(r_c) > 1$ is mean compared fails

APPENDIX B

Table 1b Criteria of acceptability for photon dose calculations, for the dose deviation, for the various regions in a phantom beam [18, 19].

	region	Homogeneous simple geometry	Complex geometry (wedge, inhomogeneity, asymmetry, block/MLC	More complex geometry
δ_1	central beam axis data-high dose, low dose gradient	2%	3%	4%
δ_2[a]	Build-up region of centralaxis beam,penumbra region of profile-high dose, high dose gradient	2mm or 10%	3 mm or 15%	3 mm or 15%
δ_3	Outside central axis beam region-high dose, low dose gradient	3%	3%	4%
δ_4	Outside beam edges-low dose, low dose gradient	30% (3%)[b]	40% (4%)[b]	50% (5%)[b]
RW_{50}[a]	Radiological widge-high dose, high dose gradient	2 mm or 1%	2 mm or 1%	2 mm or 1%
$\delta_{50\text{-}90}$	Beam fringe-high dose, high dose gradient	2 mm	3 mm	3 mm

[a] These values are preferably expressed in mm. A shift of 1 mm coresspoonding to a dose variation of 5% is assumed to be a realistic value in the high dose, large dose gradient region.

[b] This percentage is applicable to the following equation $\delta_4 = 100\% \times (D_{calc} - D_{meas}) / D_{meas,cax}$, where $D_{meas,cax}$ is the dose on the central axis, since it is not always practicable to compare with the local dose. The values in bracket are those determined from the following equation $\delta = 100\% \times (D_{calc} - D_{meas}) / D_{meas}$

Where, the regions of validity of the criteria δ_1-δ_4, radiological width RW_{50}, and beam fringe $\delta_{50\text{-}90}$ are shown in graphical examples of percentage depth dose (PDD) and beam profiles of Figure 1b.

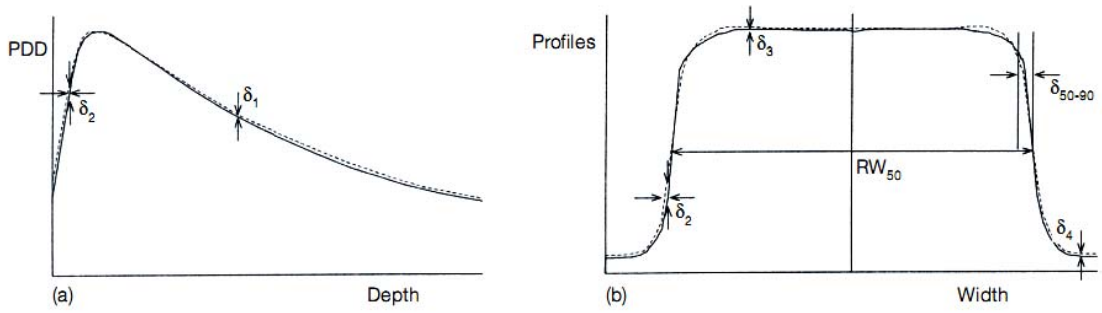

Figure 1b Regions of different accuracy capabilities for photon beam dose calculations. Reproduced, with permission, from Ref. (18). (a) Dose versus depth (PDD); (b) dose versus distance across the beam (beam profiles).

APPENDIX C

Table 1c Acceptance criteria of gamma value for 3% dose difference and 3mm DTA [20]

Value	Range	Appraisal and approach
$\gamma_{1\%}$ (1% of points have an equal or higher gamma value)	0-1.5	Accepted
	1.5-2	Acceptable, other verification tools such as angle distribution, dose difference map, and profiles are need for further evaluation
	>2	Not acceptable – measurement has to be repeated; if acceptance criteria still not fulfilled, plan has to be re optimized
γ_{mean} (mean value in gamma distribution)	0-0.5	Accepted
	0.5-0.6	Acceptable, other verification tools such as angle distribution, dose difference map, and profiles are need for further evaluation
	>0.6	Not acceptable – measurement has to be repeated; if acceptance criteria still not fulfilled, plan has to be re optimized
$\gamma > 1$	0-5%	Accepted
	5-10%	Acceptable, other verification tools such as angle distribution, dose difference map, and profiles are need for further evaluation
	>10%	Not acceptable – measurement has to be repeated; if acceptance criteria still not fulfilled, plan has to be re optimized

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