DOSIMETRIC VERIFICATION OF INTENSITY MODULATED RADIATION THERAPY TREATMENT PLANS WITH GAFCHROMIC EBT FILM USING 6 MV PHOTONS

by

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Specially dedicated to my beloved mother who passed away in Dec 2004 due to cancer.

May her soul rest in peace.

***May everyone in this world be well and happy*.**

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LIST OF ABBREVIATION

Abbreviation	Meanings
EBT	External beam therapy
IMRT	Intensity modulated radiotherapy
MLC	Multi-leaf collimator
2DXRT	Two dimension external beam
3D-CRT	Three dimension conformal radiotherapy
OAR	Organs at risk
TLD	Thermoluminiscent dosimeter
OD	Optical density
SRS	Stereotactic radiosurgery
ISP	International Speciality Products
CCD	Charge couple device
Dpi	Dot per inch
RF	Radiofrequency
CT	Computed tomography
SSD	Source to surface distance
RGB	Red green and blue
PDD	Percentage depth dose
pv	Pixels value
ADC	Analog to digital conversion
ROI	Region of interest
CL	Confidence limit
SAD	Source to axis distance
DTA	Distance to agreement
TPS	Treatment planning system

ASTRO	American Society for Therapeutic Radiology and Oncology
DVH	Dose volume histogram
QA	Quality assurance
1D	One dimension
2D	Two dimension
3D	Three dimension
Ca	Cancer

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Abstrak

Dalam projek ini, ciri-ciri filem Gafchromic (jenis EBT) diselidik sebagai alat penguji untuk jaminan kualiti. Ciri-ciri dosimetri filem EBT dianalisis sebelum digunakan dalam pengesahan dos IMRT. Filem ini diimbas dengan pengimbas dokumen Epson V700 dan kemudian dianalisis dengan meggunakan perisian Image-J dan Omni-pro. Evaluasi juga dijalankan untuk mengetahui sifat-sifat pengimbas serta perisian yang digunakan. Kalibrasi filem menggunakan ketumpatan optik terhadap dos juga diselidik, dalam julat dos yang digunakan dalam radioterapi IMRT di Hospital Kanser Mount Miriam.

Kajian ini telah menunjukkan bahawa EBT Gafchromic sesuai untuk digunakan sebagai pengukuran meter dos yang tidak bersandar kepada tenaga sinaran, sinaran dan sudut semasa penyinaran. Hubungan kalibrasi filem bagi ketumpatan optik terhadap dos adalah dalam bentuk polinomial. Protokol yang sesuai telah dicadangkan untuk semua proses, prosedur dan penilaian semasa menggunakan pengimbas dan perisian Image-J serta Omni-pro. Kajian untuk perbandingan lima kes IMRT dengan TPS dan filem Gafchromic EBT, menghasilkan nilai purata 86.65 % dengan sisihan piawai 4.2 % untuk kriteria gamma 3 % / 3 mm DTA. Bagi lima kes lain pula, perbandingan IMRT verifikasi TPS dengan Gafchromic EBT film dan 2D-array MatriXX pula, kajian ini memperoleh 88.30% untuk film Gafchromic EBT sementara 2-D array MatriXX mendapatkan 94.71% yang menggunakan kriteria gamma 3 % / 3 mm DTA. Sebagai kesimpulan, dosimetri filem ini menunjukkan resolusi ruang yang tinggi untuk pengesahan IMRT dalam kejituan ±3 % dan paras kepercayaan yang mencecah 88 % telah distandardkan sebagai kriteria untuk kawalan mutu IMRT sebelum radioterapi dimulakan. Demi mencapai paras kejituan ±3 %, aspek tertentu seperti kes tertentu yang mempunyai perbezaan dos yang tinggi perlu diubahsuai apabila menggunakan paras keyakinan 88%.

Dosimetric Verification of Intensity Modulated Radiation Therapy Treatment Plans with Gafchromic EBT Film using 6 MV Photons.

Abstract

In this project, Gafchromic film (type EBT) as an evaluation tool for quality assurance was studied. The dosimetric features of a EBT film was analysed before it was used in IMRT dose verifications. The film was scanned using an Epson V700 document scanner and then analysed using Image-J and Omni-pro softwares. The characteristics of the scanner using these softwares were also evaluated. The film was calibrated using optical density against dose in the dose range used in IMRT radiotherapy at the Mount Miriam Cancer hospital.

The study has shown that the Gafchromic EBT film is suitable as a dose measurement dosemeter as it was energy, field size and angular independent. However calibration of optical density against dose had a polynomial curve relationship. A standard protocol was created for the hospital to standarize the procedure and verification process using the scanner and software Image-J as well as Omni-pro. For five IMRT plans, dose plans from TPS and Gafchromic EBT film, a mean value of 86.65 % with a standard deviation of 4.2 % was obtained at the gamma criteria of 3 % / 3 mm DTA. For another 5 IMRT plans, dose plans from TPS versus Gafchromic EBT film and 2D-array MatriXX, gave 88.30 % for Gafchromic EBT film while 2-D array MatriXX gave 94.71 % at the gamma criteria of 3 % / 3 mm DTA. As a conclusion, film dosimetry presents a high spatial resolution for IMRT verification within an accuracy of ±3 % and the confidence level of 88% was standardized as passing criteria for IMRT QA before the patient treatment can proceed. However in certain cases where there are high dose gradients, the confidence level has to be modified to achieve ±3 %.

Chapter 1: Introduction

1.1 Introduction

The main objective in radiotherapy is to deliver a maximum homogeneous radiation dose to a target tumor volume while minimizing dose to the surrounding critical organs and normal tissues. Conventional external beam radiotherapy can achieve this but at most of times an unnecessarily large volume of normal tissue may be irradiated as the beam has to pass through healthy body tissues to reach the tumor sites [1].

Three-dimensional conformal radiotherapy (3D-CRT) is an advanced form of external beam radiotherapy. It requires 3D computerized radiotherapy treatment planning systems with immobilization devices (patients need to be fixed during treatments with mould or cast) and multi-leaf collimators (MLC) are normally used to block critical structures containing either normal tissues or normal critical organs. The radiation beams typically have uniform intensity across the fields. Wedges and compensating filters may also be used to modify beam intensity and to compensate for missing tissues.

The term intensity modulated radiotherapy (IMRT) refers to an upgraded subset of 3D-CRT which employs non-uniform dose distributions to provide an acceptable target dose whilst dose to organs at risk (OAR) is reduced. Suitable dose intensities are determined by using various computer-based optimization techniques. Dose intensity patterns can be delivered with the aid of MLCs' creating segments. Here the thickness of a region of interest (tumor) is considered and also a lower intensity is created for the normal tissue. The goal is to have a uniform dose closely following the shape of the tumor. The intensity of beams will be reduced if they pass through a missing tissue or a sensitive structure and vice versa [B1].

Conventional measuring methods such as ionization chambers, semiconductors, thermo luminescent dosimeter (TLDs) and silver halide radiographic films are not able to

measure doses absorbed in high-gradient regions of the beams. Ionization chambers and semiconductors do not have sufficient spatial resolution for isodose and depth-dose measurements. Thermoluminescent dosimeters, even with small dimensions, are time consuming when two-dimensional dose distributions are required. The silver-halide radiographic film has large sensitivity differences to photon energies in the l0-200 keV region [2]. However it offers a relatively high spatial resolution when compared to most other radiation measuring systems. Energy absorption properties of radiographic films do not match exactly those of biological tissues. Radiographic film is sensitive to room light and requires wet chemical processing in the dark. This difficulty has resulted in a search for a radiation dosimeter with high spatial resolution, insensitive to light and has a permanent record of the measurement. It must have an acceptable accuracy and precision. Some of these features have been achieved with the introduction of radiochromic film dosimeters.

Since 1965, detailed studies have been performed by many authors [1-19] to determine the dosimetric properties of the various forms of radiochromic dosimeters. Much of the work has been performed at the U.S. National Institute of Standards and Technology with the support from the Division of Isotopes Development, U.S. Atomic Energy Commission, and with the assistance of the inventor of ultraviolet sensitive systems [5]. With the recent improvements in the accuracy and precision of film manufacturing, the films have become increasingly popular in medical and nonmedical applications. Over the past several years the dosimetric properties of radiochromic films have been evaluated by many investigators [1-19] and extensive literature on various aspects of radiochromic dosimetry has been reported. At present, various radiochromic dosimeters in the form of thin films and thick films are used for routine dosimetry of ionizing radiation over a wide range of absorbed doses (1-10 Gy) and absorbed dose rates (up to » 10^{12} Gy s^{-1}).

Each IMRT plan is required to have a QA verification as high dose gradients are present in an IMRT plan . An IMRT QA reveals the dosimetric differences between plans from a treatment planning system and measurements. The Gafchromic EBT film was chosen because the film has a high spatial resolution and a relatively low spectral radiation sensitivity variation. The film is insensitive to visible light, thus it is easy to handle and prepare in room light. Radiochromic film changes color when exposed to radiation and does not require chemical processing. Image formation is due to polymerization process, when energy is transferred from an energetic photon or charged particle to the receptive part of the leuko-dye or colorless photo monomer molecule. This initiates a color formation through chemical changes. The characteristics of Gafchromic EBT films such as post-exposure density growth, photon energy dependence, field size dependence and set-up had to be investigated before the film can be used as a standard for IMRT QA.

In order to systematically understand the factors influencing the characteristics of Gafchromic EBT films, a detail study of all instruments and softwares used was performed to standardize the protocol. In order to optimize the scanning system, the effect of scanning direction, the necessary RGB mode and the scanner uniformity were studied. Many authors [2, 6-12], have reported that all these tests have to be performed so that Gafchromic film can be used as a dosimetry tool in IMRT verification. In this research, all the tests used by all investigators [6-12] will be optimised and standardized so that the film can be used as a standard protocol or procedure for IMRT QA in the Mount Miriam Cancer Hospital, a non-profit hospital in Malaysia.

The gamma criteria which is used to compare the dosimetric differences between plans in treatment planning system and measurements has to be determined. Two dosimetric parameters, dose difference and distance-to-agreement (DTA), are frequently used to evaluate the agreement between planned and delivered IMRT fields. According to some researchers, [20-22] a 3% dose difference and 3mm DTA in the planned and

delivered IMRT fields constitute acceptable agreement between the two types of fields. Another widely used IMRT QA analysis tool, the gamma index or criteria (γ), also takes into account both dose difference and DTA. A γ of 1.0 or less indicates that a particular point falls within the 3% dose difference and 3 mm DTA criteria and, therefore, is an acceptable result. After the gamma criteria is fixed, the confidence limit has to be ascertained so that all QA that passed this standard acceptance criteria can then be followed up for treatment.

1.2 Objectives of the study

- To study the characteristics of Gafchromic EBT film using a 6 MV photon beam
- To evaluate the characteristics of EPSON V700 scanner and the Omni-Pro as well as Image-J softwares for digitizing the films
- To develop a verification process and quality assurance method for IMRT
- To determine a confidence level for a standard protocol used in the Mount Miriam Cancer Hospital.

CHAPTER 2

LITERATURE REVIEW AND THEORY

2.1 Introduction

Accurate dose measurement is needed for the validation of dose calculation algorithms used in IMRT treatment planning. IMRT is particularly used in treating sites, such as the head and neck, breast and chest wall (if there is total mastectomy). These sites have organs at risk (OARs) near the target volumes. Dose calculation algorithms used to optimize dose distributions are via inverse planning techniques. Step-and-shoot intensity modulated radiation therapy (IMRT) fields resulting from inverse planning are essentially a collection of small fields grouped to yield a larger modulated field. The surface dose is strongly dependent on the treatment parameter settings for IMRT fields.

The switch of head and neck treatment from conformal radiation fields to IMRT has resulted in less critical organ toxicity. This reduction is due to improved immobilization techniques (masks) combined with the use of multiple fields in IMRT. This effectively increases the dose to the target. However, it has been reported that the IMRT fields increase near-surface dose compared to conformal fields [3]. The increased skin dose in IMRT is attributed to several extrinsic factors, such as oblique incidence of beams, the use immobilization devices and the proximity of target volumes to the surface [4].

Each field in IMRT becomes a unique “painting” of intensity, optimized for a specific patient’s anatomy, beam angle, and planned dose distribution. The dose-calculation algorithms of the TPSs become more complicated as there are many small and irregular subfields. Due to the inherent assumption in inverse planning that the calculation used for optimization has to be accurate in the first place [23]. However, despite the development of new delivery and planning tools, the development of efficient and thorough IMRT QA tools

lagged slightly at first, leaving medical physicists to do their work with the limited tools available to them.

These new clinical and practical needs created a niche for commercial IMRT QA products and subsequently a set of IMRT QA systems emerged. Systems for IMRT QA are now a staple of modern clinics and they have continued to evolve as the increasing usage of IMRT has precipitated a need for greater efficiency and more advanced features. Over the past few years, many reseachers [5,6,13] have shared this set of fairly uniform commercial systems and strategies for IMRT QA. As a result, IMRT programs today almost universally have a quantitative comparison between TPS planar dose and measured dose which generate statistics of calculations such as percentage difference, distance to agreement (DTA), and gamma criteria analysis [22].

This first stage of IMRT QA evolution hinged on the wide acquisition and implementation of the new IMRT QA systems. These systems include film scanning and calibration, ion chamber arrays, diode arrays, and more recently, megavoltage electronic portal imaging devices [20] have become regular tools in the modern IMRT clinic. Three general goals worth considering next would be to improve the understanding of current tools and analysis methods. This task include refining them to be as intuitive, efficient, and meaningful as possible. Secondly is to improve existing tools and to develop new tools to continue to meet the needs of advances in TPSs, delivery and image-guided radiation therapy. Thirdly, to propose, prove, and implement universal IMRT QA standards based on experience and relevant clinical endpoints.

AAPM Task Group 119 [5] has produced quantitative confidence limits as baseline values for IMRT checking. A set of test cases was developed to assess the overall accuracy of planning and delivery of IMRT treatments. Each test uses the contours of targets and avoidance structures drawn within a rectangular phantom. This tests are planned, delivered and measure using different modalities of dosimeters. Each facility

must pass the Radiological Physics Center credential tests for IMRT. The agreement between the planned and measured doses is determined by using ion chamber and film. Ion chamber is used in high and low dose gradient regions meanwhile film is used in coronal planes inside the phantom where all the fields are delivered. Planar dosimetry for each field is measured perpendicular to the central axis. The planar dose distributions are assessed using gamma criteria of 3%/3 mm [5].

2.2 Gamma Criteria

The quantitative comparison of dose distributions by calculation using algorithmns in treatment planning system or using Monte Carlo simulation versus measured data has become a key issue in multidimensional dosimetry in the implementation of IMRT. Simple evaluation by superimposing isodose distributions can only highlight or indicate areas of disagreement but does not allow the level of agreement/disagreement to be specified in a quantitative way. The most often applied dose evaluation tools comprise a direct comparison of dose differences, a comparison of distance-to-agreement (DTA) between measured and calculated dose distributions and a combination of these two parameters which is the gamma evaluation method. Besides these three commonly applied methods, other dose evaluation tools have also been proposed such as the confidence interval method [24], the normalised agreement test [25] and the dose-gradient compensation method [26]. Dose differences can be expressed in many ways. Sometimes the absolute value of the dose difference is of interest, but generally the difference is normalised to the dose having a specific value, for instance the prescribed dose, the maximum dose or the dose on the beam axis at the same depth. It should be clear that such a normalisation is not reflecting the local dose difference, which might be a quantity more relevant for organs at risk. In regions of low dose gradients it is sufficient to evaluate dose differences independently of spatial considerations. In regions of high dose gradient, (normalised)

dose differences are less meaningful but instead should be translated into a DTA, which is applied in reports on quality assurance of treatment planning systems [20, W13, 27]. These two approaches have to be adopted for the verification of separate intensity modulated beams or composite (multi-beam) treatment plans where low-dose gradient and high-dose gradient regions can alternate. For that purpose, some investigators have proposed the γ-evaluation method for the quantitative evaluation of two-dimensional dose distributions [23, 24].

This concept combines a dose-difference criterion with a distance-to-agreement criterion for each point of interest. Since its introduction, the γ-evaluation method has been used for the commissioning of IMRT equipment and patient-specific quality assurance procedures. Refinements on the gamma evaluation and its application have also been described. Here the authors applied the γ-evaluation method for the verification of single IMRT beams with an electronic portal imaging system [21]. They categorised the evaluated points at different filter levels either to reduce the amount of calculation time or to use linear interpolation for suppressing artefacts. They then proposed to reduce the continuous nature of the γ-value to a pass-fail decision for each point of interest. Through this method a map of passed or failed points is obtained but the quantitative information regarding the numerical γ-value, is lost. One of the authors revised the γ-evaluation method by introducing dose-gradient dependent local acceptance thresholds [28]. Other researchers examined the behaviour of the γ-distribution in the presence of noise when introduced in Monte Carlo dose calculations and evaluated the influence of pixel spacing [29]. In order to avoid artefacts in the γ-calculation in regions with steep dose gradients, the resolution of the dose Matrix and the DTA-criteria have to be considered. Based on their analysis [29], it was recommended a minimum ratio of 1:3 between pixel resolution and DTA criteria. Besides the correct application of the concept and definition of tolerance and acceptance criteria, the interpretation of a two- or more-dimensional γ-value matrix is

essential. Another investigator [30], investigated 10 IMRT hybrid plans and verified them with films in a polystyrene phantom. Based on the results of these plans with measurements in 3 planes, they developed a decision filter at γ mean values, the average number of pixels with γ > 1, and the maximum γ value expressed as the 1st percentile (γ1%). In addition, γ-area histograms were used for each plane where a comparison between calculated and measured dose distributions was performed. In this way, a reduction of the multi-dimensional information concerning the agreement between a reference (measured) and an evaluated (calculated) dose distribution seems to be feasible. From either γ-area distributions or histograms statistical data can be calculated to define acceptance criteria for either composite IMRT plans or single IMRT beams. Nevertheless, a thorough experimental IMRT-verification needs more than the calculation of the γ-distribution.

Complementary dosimetric information, such as dose profiles and dose-difference maps, should be considered as well in a quantitative analysis of multi-dimensional dosimetric information. Definitions need to be determined for dose difference and isodose distance as a pass or fail criteria. If both parameters (dose and isodose distance) are outside their pass or fail criteria, the agreements “fails” according to the gamma method. If only one parameter is outside the defined pass or fail criteria but the others are well inside, the IMRT plansare acceptable. In addition to the calculation of the γ-index, other researchers [48] have looked at the γ-angle (see Fig 2.1). If D_m is the measured dose at co-ordinate r_m , D_c the calculated dose at co-ordinate r_c , ΔD_m the dose-difference tolerance criterion and Δd_m the distance-to-agreement tolerance criterion, the gamma value for the measurement point r_m is defined as:

$$\gamma(r_m) = \min\{\tau(r_m, r_c)\} \forall \{r_c\} \quad (2.1)$$

where

$$\tau(r_m, r_c) = \sqrt{\frac{r^2(r_m, r_c)}{\Delta d_M^2} + \frac{\partial^2(r_m, r_c)}{\Delta D_M^2}}$$

$$r(r_m, r_c) = |r_c - r_m|$$

and

$$\partial(r_m, r_c) = D_c(r_c) - D_m(r_c)$$

The pass-fail criteria are:

$\gamma(r_m) \leq 1$ calculation passes

$\gamma(r_m) > 1$ calculation fails

This gamma calculation is then performed for all r_m

r_m : position of a single measurement point (set into the origin for this calculation)

r_c : spatial location of the calculated distribution relative to the measurement point

Δd_M : passing criteria for isodose distance

ΔD_M : passing criteria for dose

$D_c(r_c)$: calculated dose in r_c

$D_m(r_c)$: measured dose in r_m

[B7]

The γ-angle can be useful for the interpretation of deviations. It indicates the parameter mostly influencing the γ-value, *i.e.* either the dose difference or the DTA as shown in Fig 2.2.

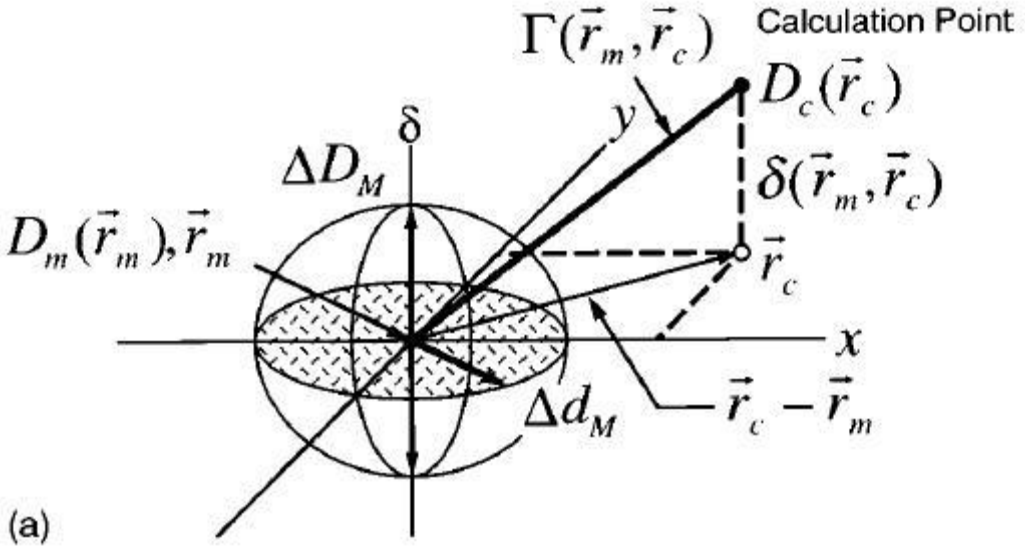

Fig 2.1: Definition of the gamma value, γ *(r_m ,r_c),* and gamma angle

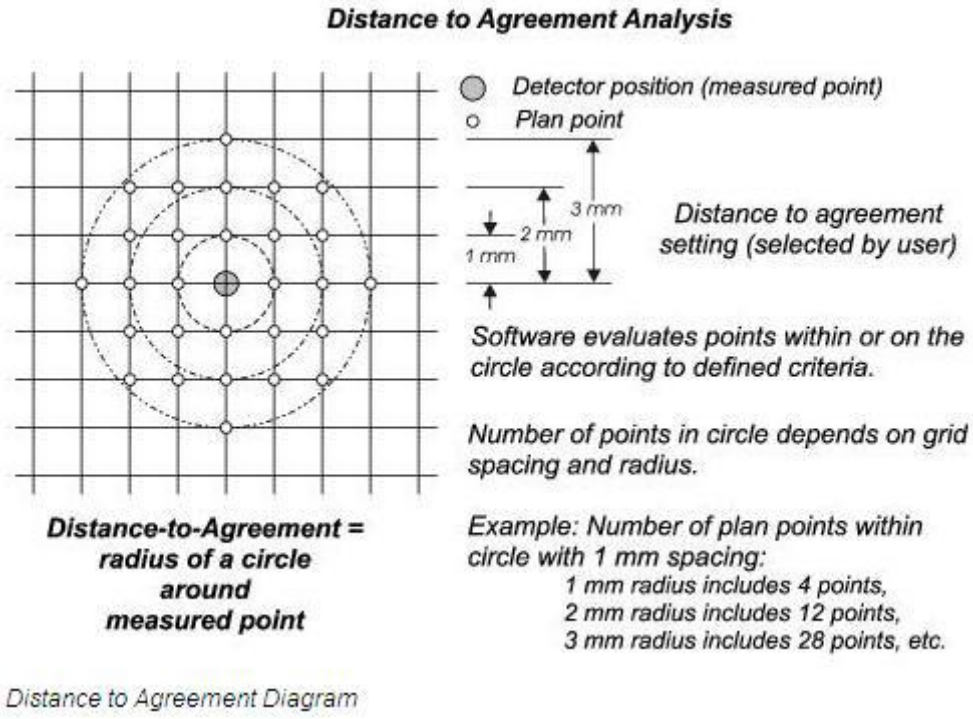

Fig 2.2 Distance to agreement analysis DTA [W14]

The angles of 0° are defined on the dose-difference axis. For example, if the γ-angle is between π/4 and π/2 the index is dominated by the DTA criteria. The angle is calculated with the absolute values of dose-difference and distance-difference so that the angle is always between 0 and π/2. Such information is lost if only the absolute value of gamma is considered. The planes used for analysis is important in determining the percentage of points passing the gamma criteria. Examples include using a region of interest or a threshold to exclude some points from the assessment and normalizing the measurements to some reference point, and defining the percentage agreement in terms of prescription dose. In practice, physicists use commercial software that have different available options and so it is difficult to offer definitive guidance regarding acceptance levels for gamma analysis results. It seems reasonable, however, to expect that if one normalizes the film results to ion chamber measurements in the high dose region on the same plane, then on average about 95% of the points on the plane within the region of interest should pass gamma criteria of 3%/3 mm with a confidence limit that ranges down to 88%.

Radiographic silver halide film dosimetry provides a fast, convenient method of measuring 2D dose distributions in megavoltage radiation beams. However, the disadvantage is the energy dependence of film and processor variation induced error. Many recent studies have been performed to investigate the use of radiochromic films for IMRT dose distribution evaluation.

2.3 Film Dosimetry

2.3.1 History

Many companies such as Kodak, Agfa, Fuji and Dupont have contributed to the historical development (Kodak 1999) of radiographic films. The first photographic emulsion film was made in 1826/1827 by the French scientist J. N. Niepce, and it took eight hours of exposure time. In 1839, another French scientist, L.J.M. Daguerre, introduced the concept of developer. In 1889, Eastman Kodak introduced the cellulose nitrate base for emulsion. In 1895, Wilhelm C. Roentgen discovered a “new kind of light”, which he named “X-rays.” He made the first radiograph of the hand of Mrs. Roentgen on a glass plate.

In 1972 radiographic films such as XOMAT-TL and XOMAT-V were introduced for tumor localization in radiotherapy and for dosimetric verification. In 1997, the Kodak ECL film system for oncology was introduced, which provides high-contrast images for monitoring radiation treatment of cancer patients. The period 2000-2001 is characterized by film digitisation. In 2001 the new Kodak ready pack film called “extended dose range” or EDR2 for dosimetric verification was introduced. In present-day practice, films used for oncology are localization films (e.g. Kodak EC-L, Kodak XOMAT-TL), simulation films (Kodak TGmat plus) as well as verification films (XOMAT-V, EDR2). Localization means the spatial delineation of the tumor, simulation is the assessment of optimal treatment geometry using an orthovoltage X-ray source and verification is the quality control of the high-energy photon or electron beam during treatment.

Colorless transparent radiochromic thin films giving permanently colored images have been widely used for 30 years as high-dose radiation dosimeters. These are mainly hydrophobic substituted triphenylmethane leucocyan dyes, which upon irradiation undergo heterolytic bond salts scission of the nitrile group to form highly colored dye in solid polymeric solution. The host material for such films is generally nylon, vinyl, or styrene-

based polymer. They have also been used to register high-resolution, high contrast radiation images and to map radiation dose distributions across material interfaces. This kind of radiochromic system was not sensitive enough to be used in clinical or radiological applications. Recently, another form of radiochromic film based on polydiacetylene has been introduced for medical applications. These films were previously supplied in two types, GafChromic DM-1260 (also known as HD- 810) for nomenclature designation and single-layer GafChromic MD-55 for the absorbed dose ranges 100-500 Gy [W2] and l0-50 Gy [W3], respectively. A new double-layer GafChromic MD-55 film has now replaced these films for medical applications (useful dose range from 1-100 Gy). Each of these film types is colorless before irradiation. It consists of a thin, active microcrystalline monomeric dispersion coated on a flexible polyester film base. It turns progressively blue upon exposure to ionizing radiation. The new Gafchromic EBT dosimetry film has been developed specifically to address the needs of the medical physicist and dosimetrist working in the radiotherapy environment. In common with previous radiochromic films, EBT film is self-developing but it also incorporates numerous improvements in radiochromic film technology. Gafchromic EBT dosimetry film has been in clinical and field evaluation for nearly 1 year before it was officially launched at ASTRO in October 2004 [W4].

2.4. Fundamental Film Dosimetry

Many authors [4,5,7,8] have suggested different equations for the nonlinear relation between net optical density and dose. One of the investigator [6] have suggested the interaction of photons with the active component in EBT, is expected to follow Poisson statistics. By applying the single hit theory, the relation between optical density (OD) and the dose (D) is given by

$$OD = \frac{c_1}{2(c_2 / c_1)}\{1 - \exp(-2(c_2 / c_1)D)\} \quad (6)\ (2.2)$$

where c_1 is expressed in terms of Gy^{-1} and c_2 in terms of Gy^{-2}. In equation 2.1, c_1 is given as the "sensitometric slope" and c_2/c_1 as the "sensitometric curvature". Both c_1 and c_2/c_1 can be determined from fitting experimental data.

For a general theory of single-target single-hit model, the single-target single-hit model assumes that at least one event is necessary for the formation of a speck in the silver grain to achieve a probability of development.

$$\boldsymbol{N/N_o = 1 - e^{-R}} \text{ (the proportion of developed grains)} \quad (2.3)$$

where N is the number of developed grains per unit area, N_0 is the total number of grains per unit area in the emulsion, and R is the average number of events per grain. The average number of events (R) increases with increasing dose. In addition to dose dependence of R , investigators have reported that a dose rate dependence exists for radiographic film [31-33]. The dose rate dependence is a minor effect compared to the dose dependence and it can be neglected.

The film processing conditions could affect the average number of events (R) and change the number of developed grains. Therefore, R could be written as:

$$R = \gamma\varepsilon\mu D_w \quad (2.4)$$

where D_w = dose to water, μ = the energy dependence factor due to the photoelectric effect in film response (μD_w : dose to film), E= film intrinsic sensitivity to the radiation dose, and γ= film processing effect. The optical density (OD) is used to describe the darkness of the film and is defined as:

$$OD = \log_{10}(I_0 / I) \tag{2.5}$$

where I_0 is the incident light intensity measured in the absence of film and I is the intensity transmitted through the film. Then, the OD can be written as

$$OD = \log_{10}(e^{N\sigma}) = (\log_{10} e)N_0\sigma(1 - e^{-R}) = OD_{\max}(1 - e^{-\alpha D}) \tag{2.6}$$

where σ is the effective area of a silver grain, OD_{max} is equal to ($\log_{10}$ e) N_0 σ and would be constant for a constant number of grains in the emulation, and α is equal to γ+μ which depends on the film processing conditions, film specific sensitivity and energy spectrum. Due to the limitation in the scanner (for example, the nonlinearity at large OD and saturation at OD ~3.6 for the Lumisys scanner), it is difficult to acquire true OD_{max} for high-dose beam delivery. A possible way of acquiring OD_{max} is through fitting the calibration curve with the above model equation(2.6).

The uniformity in the horizontal direction for the Lumiscan75 laser scanner is within 1% variation compared to the value at the center of the scanning region. The linearity of the scanner was evaluated with R-squared of 0.997 for OD range between 0.2 and 3.0. Thus, the calibration curve (pixel value versus dose) in this study can also be described by the single-target single-hit model (Eq.2.3). The equation can be transformed as:

$$P = P_0 + P_s(1 - e^{-mD/P_s}) \tag{2.7}$$

where P is the total pixel value, P_0 is the background pixel value, P_s is the saturation pixel value, m is the film sensitivity slope parameter in pixel value/cGy, and D is the dose in cGy. The background pixel value (P_0) is due to film fog and base layer. If all silver grains were developed and the concentration of grains is assumed constant, P_s can be assumed constant for each batch of film. The film sensitivity slope parameter (m) represents the initial slope of the response curve and depends on radiation type, energy, depth, field size,

dose rate, film orientation and film processing conditions. The *m* parameter could be written as:

$$m(E, FS, d, FP) = m_E(E, FS, d) \cdot m_{FP}(FP) \tag{2.8}$$

where *E* , *FS* , *d* and *FP* are the energy, field size, depth and film processing conditions, respectively. When the radiation type, machine output (MU/min) and film orientation are the same, m_E (*E* , *FS* , *d*) is a constant, independent of film processing conditions. The ratio of the *m* parameter in any irradiation condition to a reference condition can be determined at the same time (with less variation in film processing conditions) and the influence of m_{FP} can be removed. Then, the *m* ratio for any irradiation condition is constant. The *m* parameter and whole calibration curve can be known for any irradiation condition when the reference calibration curve is acquired [33].

Meanwhile, another investigator [7] had suggested

$$OD = \log \frac{2^{16}}{pv+1} \tag{7) (2.9}$$

where pv is pixel value from the scan film. Since the measured pv of irradiated films had proven stable and highly reproducible even for different sheets of film, no correction is needed for the fog readings. The mean value of the pvs measured before irradiation for all film pieces used for a specific sensitometric curve was included as the first point (corresponding to 0 cGy) in the sensitometric curve. Thus, for all the experiments done in this research using EBT films, the optical density was calculated with equation 2.8.

The OD versus exposure curve is uniquely defined for each film which is known as the blackening curve or the sensitometric curve or the H&D curve that stands for its inventors Hurter and Driffield in 1890. The response curve of radiographic film for film screen systems has a sigmoid shape and is divided into toe, slope and shoulder regions.

This slope is an important factor that describes the sensitivity of a film. In dosimetry, the blackening curve should be approximately linear with dose and approximately independent of the dose rate and radiation energy. The OD of dosimetric films depends on film storage, processing and reading conditions. Even though there are several types of films available, Kodak films account for 95% of the films used for dosimetry of ionising radiation. Two most commonly used films are XOMAT-V and EDR2 in therapy and verification, serving as “fast” and as “slow” (highly sensitive and moderately sensitive) films. These films are individually wrapped in light tight envelopes. Due to the high atomic number of emulsion components such as silver (Ag), bromine (Br) or iodine (I), this film has a photon energy dependence which causes serious problems in the dosimetry of kilovoltage beams but to a lesser degree in megavoltage beams [8]. However in the megavoltage range, film sensitivity may be influenced by the presence of low energy scattered photons. Radiochromic film such as Gafchromic EBT is energy independent and requires no chemical processing. This high sensitivity radiochromic film has been designed for the measurement of absorbed dose of high-energy photons used in IMRT as well. This film has a dose range from 1 cGy to 800 cGy dose range. The response of photons from MeV to about 30 keV reveals that the sensitivity of film changes by less than 10% [W5].

2.5 Radiotherapy

Radiation therapy uses high-energy x-rays (ionizing radiation) to stop cancer cells from dividing. A centiGray (cGy) is the scientific unit of measure for absorbed radiation energy. A patient who undergoes radiation therapy for cancer will receive several thousand cGy over a very short period of time (weeks or months). During radiation therapy, x-rays deposit energy in the area being treated damaging the genetic material of cells and making it impossible for these cells to divide or grow. Although radiation damages both

cancer cells and normal cells, the normal cells are usually able to repair themselves and function properly. Like surgery, radiation therapy is a local treatment; it only affects the cells in the treated area. Radiation therapy may be used to treat localized solid tumors, such as cancers of the skin, head and neck, brain, breast, prostate and cervix. Radiation therapy can also be used to treat leukemia and lymphoma (cancers of the blood-forming cells and lymphatic system) respectively.

The treatment device is a linear accelerator which delivers high energy x-rays directly to the tumor. Linear accelerators use powerful generators to create the high energy x-rays for external beam radiation therapy. The linear accelerator has a special set of lead shutters, called collimators, which focus and direct the x-rays to the tumor.

2.6 Intensity Modulated Radiation Therapy

Conventional external beam radiotherapy (2DXRT) is delivered via two-dimensional beams using linear accelerator machines. 2DXRT mainly consists of a single beam of radiation delivered to the patient from several directions, mainly from front, back, or both sides. Conventional refers to the way the treatment is planned or simulated on a specially calibrated diagnostic x-ray machine known as a simulator because it resembles the linear accelerator. Arrangements of the radiation beams will be done to achieve a desired plan. The aim of simulation is to accurately target or localize the volume which is to be treated. This technique is well established and is generally quick and reliable. But some high-dose treatments may be limited by the radiation toxicity capacity of healthy tissues which lay close to the target tumor volume. An example for this problem is in the treatment of the prostate gland, where the sensitivity of the adjacent rectum limited the dose prescribed to such an extent that tumor control may not be easily achievable. Historically, the maximum radiation dose that could be given to a tumor site has been restricted by the tolerance and sensitivity of the surrounding nearby healthy tissues. When

a tumor or condition is not eligible for treatment with normal conventional treatment, conformal radiation may be used in one or more sessions. It is only available with linear accelerator-based technology. Prior to the invention of the CT, physicians and physicists had limited knowledge about the true radiation dosage delivered to both cancerous and healthy tissue. For this reason, 3-dimensional conformal radiotherapy is becoming the standard treatment for a number of tumor sites.

3-D conformal radiotherapy (3-D CRT) is the term used to describe the design and delivery of radiotherapy treatment plans based on 3-D image data. Treatment fields are individually shaped to treat only the target tissue. Conformal radiotherapy permits the delivery of dose to the tumor while limiting the dose to normal tissue structures thus minimizing the adverse effects of treatment. Its principle merely benefits patients who receive curative radiotherapy. When radiotherapy is being given with palliative intent, the prescribed total doses are usually lower and the adverse effects of palliative radiotherapy are therefore likely to be less. For this reason conformal radiotherapy is not often used when delivering palliative treatment, although it is always desirable to minimise the volume of non target tissue that is irradiated. Conformal radiotherapy can be regarded as a step towards intensity modulated radiotherapy (IMRT) [B2].

IMRT is short for intensity modulated radiation therapy. The intensity of the radiation in IMRT can be changed during treatment to spare more adjoining normal tissue than is spared during conventional radiation therapy. Hence, an increased dose of radiation can be delivered to the tumor using IMRT. IMRT is a type of conformal radiation, which shapes radiation beams to closely approximate the shape of the tumor. Local or regional control of a tumor is the ultimate goal of an overall treatment strategy. Failure to achieve tumor control can result in a greater likelihood of developing distant metastases, continued tumor growth, severe debilitation or even death of the patient.

IMRT enables a more precise conformal radiation dose distribution to the target area by allowing the physician to control the intensity of the radiation beam within a given area. IMRT utilizes beams or multileaf collimators that can turn on or off or be blocked during treatment, varying the radiation beam intensity across the targeted field [B2].

The radiation beams may be moved dozens or hundreds of times and each may have a different intensity, resulting in radiation sculpted in three dimensions. The healthy surrounding tissue receives a smaller dose of radiation than the tumor (as shown in Fig 2.3 and Fig 2.4). Thus there is no longer a homogeneous or even radiation dose, but a dosage that can be made higher and varied within the tumor. This can be explained in terms of DVH. The purpose of a DVH is to summarize 3D dose distributions in a graphical 2D format. In modern radiation therapy, 3D dose distributions are typically created in a computerized treatment planning system based on a 3D reconstruction of a CT scan. The "volume" referred to in DVH analysis can be a target of radiation treatment, a healthy organ near a target, or an arbitrary structure as shown in Fig 2.5 and Fig 2.6. The end result is better tumor control, less damage to healthy tissues and structures in the treatment area and a better quality of life for the patient. Treatment planning for IMRT is more complex than for conventional radiation therapy. Three-dimensional planning for IMRT need more immobilisation devices such as mask or body frame compared to a simple one-slice planning for conventional radiation therapy. These devices assist the radiation delivery machines in targeting with more accuracy. Frequently, the localization device is molded to fit the precise contours of the individual patient. The molded device or body frame will be placed on the patient each time he receives a treatment. Due to precision of IMRT treatment, the patient will require more minute or thinner CT-scan slice.
Other than IMRT treatment, static radiosurgery (SRS) treatments also have the ability to deliver a higher radiation dose within the tumor and less damage to surrounding healthy

tissues. Stereotactic radiosurgery is a highly precise form of radiation therapy used primarily to treat tumors and other abnormalities of the brain.

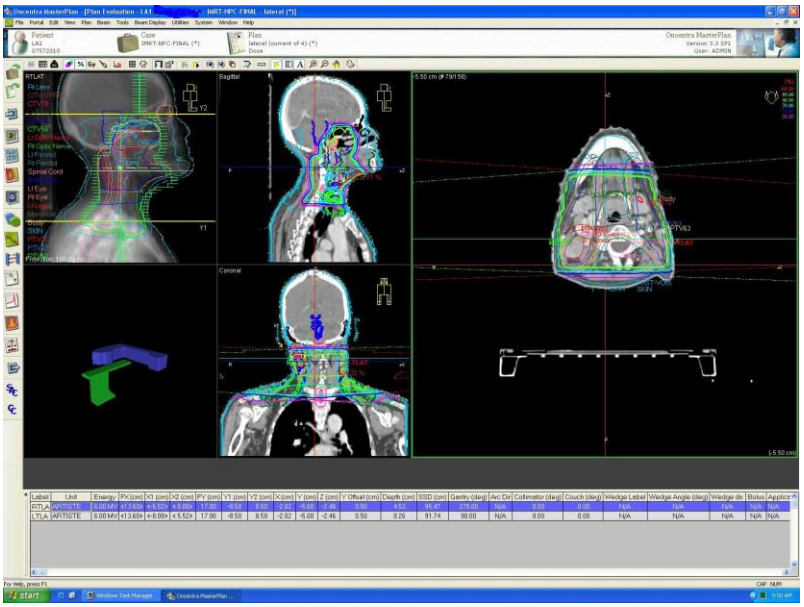

Fig 2.3: Conventional planning where most of the OAR is cover in treatment irradiation

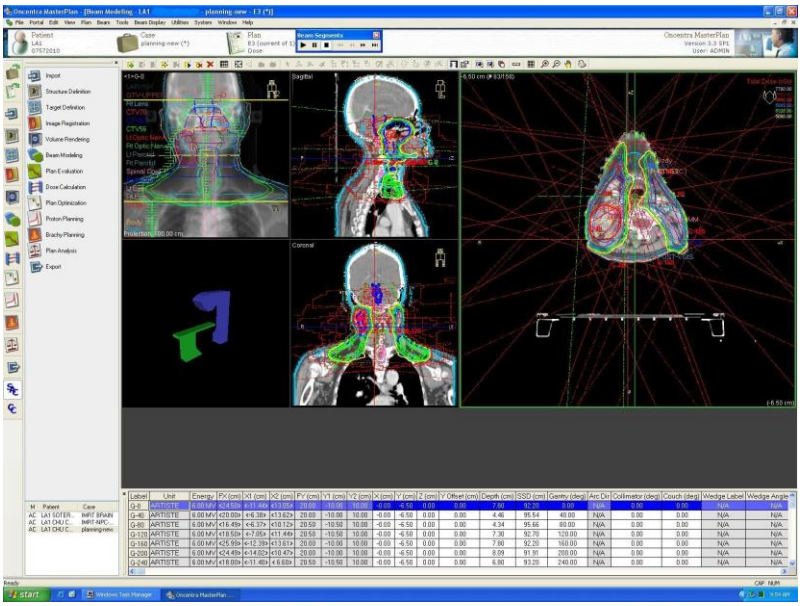

Fig 2.4: IMRT planning where OAR structures are getting less dose compared to conventional treatment planning.