THE DOSIMETRIC ANALYSIS OF TREATMENT PLANNING SYSTEM AND RADIOBIOLOGICAL STUDIES FOR THE TELETHERAPY OF LUNG TUMOURS

PhD thesis booklet

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Introduction:

The primary treatment for non-small cell lung tumours detected at early stage is surgery [1]. If the surgery cannot be applied due to the patient's general condition, old age, or comorbidities, stereotactic body radiation therapy (SBRT) may provide an equivalent alternative [2,3]. For the introduction of SBRT into clinical practice, I examined the parameters of topometric imaging, target volume determination, treatment planning, and treatment delivery.

In order to implement SBRT treatments, intensity-modulated radiation therapy (IMRT) is the most commonly used technique. IMRT plans must be verified with measurement before treatment [4]. The value of the parameter describing the similarity between the expected calculated and the actual measured dose distributions should be above a predetermined intervention level. [5]. To determine the acceptance level and the parameters to be used, we need to know the properties and limitations of the current dosimetry system. Not only the dose delivered by the treatment machine has to be considered, but also the inaccuracy of the calculated dose distribution is an important parameter. I checked the accuracy of the dose delivery with film dosimetry and electronic portal imaging device (EPID), and I determined the differences caused by the properties of the measurement systems.

The differences caused by the use of different calculation algorithms are particularly significant at the radiotherapy of the tumours in the chest. Several types of tissue (muscle, bone, lung, etc.) are present in the thoracic region, so the accurate and reliable dose calculation has high priority [6]. In my work, I compared the “Type B” Analytical Anisotropic Algorithm (AAA) and “Type C” Acuros External Beam (AXB) calculation algorithms implemented in the Varian Eclipse (Varian, Palo Alto, USA) treatment planning system using clinical beam arrangements. I also tested AXB with dose-to-water (DtW) and dose-to-medium (DtM) settings [7]. I determined the clinically relevant differences between the calculation algorithms.

In radiobiology the application of the linear-quadratic (LQ) model is the most common. Using that model and taking into account the radiobiological characterization parameters α and β, the biologically effective dose (“BED”) can be calculated, and the different fractionation schemes become comparable. Radiobiological dose estimation can be performed by analysing the chromosomal aberrations of the lymphocytes of the peripheral blood. That way it is also possible to compare the radiobiological effects of photon radiations with different energies and dose rates.

Objectives:

1. The investigation of imaging, target volume determination and treatment planning parameters required for the development of radiotherapy for small-size, node-negative lung tumours, and the introduction of the stereotactic treatment of lung tumours into clinical practice.
2. The investigation of the clinical applicability of radiochromic film dosimetry systems and EPID used for the dose verification of treatment planning systems.
3. The investigation of the effect of calculation algorithms on dose distribution in the case of SBRT of lung tumours and the determination of clinically relevant differences.
4. The comparison of the biological effects of photon beams of different energies available on a linear accelerator, based on the analysis of the number of chromosomal aberrations generated in peripheral blood lymphocytes.

Methods:

If we want more accurate information about the position of a lung tumour, we need to know which respiratory phase was acquired, or an averaging method need to be used. I compared target volumes using conventional, verbal-guided, respiratory-gated, and 4D-CT image sets. I examined the direction and the magnitude of tumour displacement, and determined the achievable planning target volume reduction by using breathing management methods. I compared the exposure from different CT imaging methods based on the displayed and measured dose values. Based on the obtained results, I determined the imaging protocol, the treatment planning procedure and the required image guidance methods used for the SBRT treatments.

I compared the planned and measured dose distributions of the intensity-modulated plans used by gamma analysis. I determined the effect of the number of monitor units, and the mean and the standard deviation values of the gantry speed and the dose rate on gamma analysis. I also analysed the effect of aperture complexity metrics (ACMs), which characterize the complexity of MLC motion. I compared the results of three image processing softwares (PTW Mephysto, FilmQA Pro, Radiochromic.com) developed for film dosimetry measurements. I also measured the dose directly with the EPID of the linear accelerator.

I performed the accuracy check of the calculation algorithms by measurements in a CIRS IMRT Thorax phantom (CIRS Inc., Norfolk, VA, USA) with a PTW 31010 semi-flexible ionization chamber (PTW Freiburg, Germany) using typical clinical beam arrangements and target volumes. I examined the effect of the size and the material of the target volume on the dose distribution. I analysed the effect of the CT number distribution within the PTV and the ITV on the dose parameters of the target volumes. I examined the dose parameters to the chest wall and determined the dependency of dosimetric parameters on the calculation algorithm.

In vitro calibration curves were defined using dicentric chromosome assay. X-rays generated by a linear accelerator using 6 and 10 MV energies were investigated. I analysed separately the effect of the flattening filter with a standard flattening filter ("FF") and flattening filter free ("FFF") mode. The irradiation was repeated using different dose rates, using 0.5, 1, 2, 3, 6, and 8 Gy dose values. The number of different types of structural aberrations was evaluated specifically for 100 cells. The linear-quadratic model was used to process the data, and the α and the β values of the dose model were determined from the recorded dose-response curves. Calibration curves for each beam were generated and compared to the literature.

New scientific results:

My research has facilitated the technical development of Hungarian radiotherapy treatments, especially with the introduction of extracranial lung stereotactic treatments, the quality of patient treatments has increased significantly. Related researches, such as the examination of lymphocytes, the comparison of calculation algorithms, and the analysis of the dose verification measurements, have facilitated the safe applicability of the newly introduced modern technique. Based on these achievements, my thesis points are the following:

T1) I developed a protocol for the acquisition of CT images reconstructing three different respiratory phases and, based on them, gated radiotherapy treatment. According to the measurements, I found that the manufacturer's estimation and the measured CTDI values are the same within 5%, and the dose of 3-phase CT is approximately one-sixth of the dose of 4D-CT. By using a 3-phase CT, the planning target volume with smaller safety margin can be reduced by a third. I found that the quality of the treatment plans is independent from the fractionation scheme. Changing the fraction dose after optimization does not reduce the accuracy of the radiation plan delivery. Based on my guidelines, we performed Hungary's first

4D-CT-based, high-dose, hyperconformal, extracranial stereotactic radiotherapy treatment at the National Institute of Oncology. Since then, we have routinely performed such treatments with similar clinical results to the data that can be found in the international literature. P1, P3, P4, P5, P6

T2) I demonstrated by measurements the clinical applicability of the EBT2 and EBT3 radiochromic films and the software used for evaluation (PTW Mephysto, FilmQA Pro, and radiohromic.com) in any combination for the dosimetric verification of radiation plans. I determined the long-term darkening curve of different colour channels. Based on my results, the gamma passing rate values calculated by FilmQA Pro are significantly higher than the values by the other two softwares. I found that during the EPID-based quality assurance measurements of stereotactic treatments the saturation of the detector should be considered. P1, P2

T3) I determined the clinically relevant differences between the doses calculated by the Anisotropic Analytical Algorithm and the Acuros External Beam, and compared their results with measured and literature data. In the case of clinical beam arrangement, I proved by measurements that the difference between the two calculation algorithms is energy dependent. I found that the chosen calculation algorithm has a significant role in the normalization of the irradiation plans and in the determination of the dose threshold of the chest wall. P7, P8, P9

T4) I found that there is a significant difference between the numbers of aberrations in the peripheral blood lymphocytes in the case of different irradiation parameters. At 100 chromosome aberrations (dicentric + ring) / 100 cells, the flattening filter free (FFF) mode has a 10-20% higher relative biological effect than the standard flattening filtered (FF) mode. The biological effect is inversely proportional to the average energy of the radiation, that way the ascending order of the analysed radiation beams, according to RBE, is the following: 10 MV, 10 MV-FFF, 6 MV, 6 MV-FFF. P10, P11

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