Verification of dose calculations in radiotherapy

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Abstract

External radiotherapy is a common treatment technique for cancer. It has been shown that radiation therapy is a both clinically and economically effective treatment for many types of cancer, even though the equipment is expensive. The technology is in constant evolution and more and more sophisticated and complex techniques are introduced. One of the main tasks for physicists at a radiotherapy department is quality control, i.e. making sure that the treatments are delivered in accordance with the dosimetric intentions. Over dosage of radiation can lead to severe side effects, while under dosage reduces the probability for patient cure.

The present thesis is mainly focused on the verification of the calculated dose. Requirements for independent dose calculation software are identified and the procedures using such software are described. In the publications included in the thesis an algorithm specially developed for verification of dose calculations is described and tested. The calculation uncertainties connected with the described algorithm are investigated and modeled. A brief analysis of the quality assurance procedures available and used in external radiotherapy is also included in the thesis.

The main conclusion of the thesis is that independent verification of the dose calculations is feasible in an efficient and cost effective quality control system. The independent calculations do not only serve as a protection against accidents, but can also be the basis for comparisons of the dose calculation performance at different clinics.

Introduction

Approximately one out of seven deaths worldwide is caused by cancer. Kamangar et al. reported that approximately 7 million people died from cancer in 2002, 11 million new cases were diagnosed and 25 million persons were living with a diagnosed cancer [1]. The corresponding numbers for Sweden the same year were 42 571 diagnosed and 21 475 deaths [2]. The incidence proportions between the most common types of cancer in the world are presented in Figure 1 together with the proportions of the same cancer types in Sweden. The incidence of cancer is higher in the more developed parts of the world with approximately 400 cases per 100 000 inhabitants in Europe 2002, compared to 70 in Africa and 120 in Asia [1]. This pattern is however not the same for all kind of cancers. The incidence of liver cancer is for example approximately 4 times higher in Asia compared to North America.

The mortality rates vary dramatically between different parts of the world. The prognosis is better in developed parts of the world than in less developed. In North America approximately 20% of the women diagnosed with breast cancer die of the disease while the corresponding number for Africa is 70%. The relative 5-year survival for different cancer diagnoses in Sweden is given in Figure 2.

The incidence and mortality rates have changed over the years. Examples are given in Figure 3 and Figure 4 for different cancer diagnoses. The incidence rates for breast, prostate and testis cancer have increased over the last 40 years. The mortality rate for testis cancer however, has dropped considerably over the time period which would indicate a development of successful treatment. On the other hand, the mortality rates for prostate and breast cancer have been stable. For stomach cancer the incidence rate and mortality rate are almost the same. This shows that these patients usually die from their

disease. The decrease in incidence of stomach cancer are the result of changes in life style, i.e. more consumption of fruit and vegetables, less consumption of salt and smoked food, and also a reduced prevalence of Helicobacter in the stomach [1].

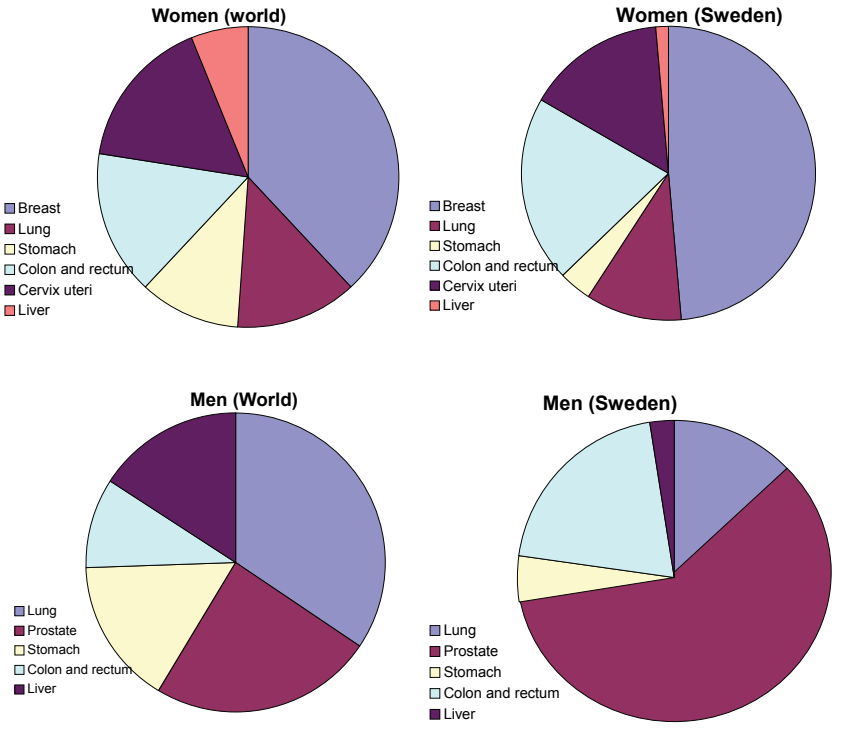

Figure 1 To the left the relations in incidence between the most common cancers in the world for women and men, and to the right the relation between the corresponding cancers in Sweden.

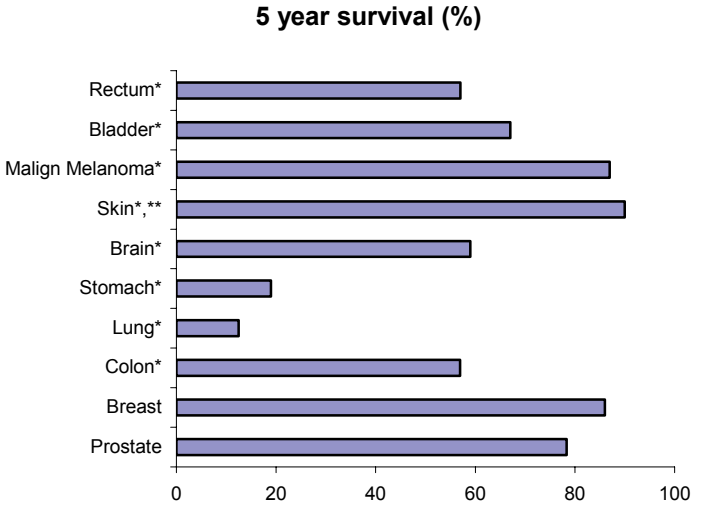

Figure 2 The relative 5-year survival for different cancer diagnoses in Sweden [3]. (*) The percentage is calculated as a mean value for men and women. (**) excluding malign melanoma.

The dominating treatments are surgery, chemotherapy, radiotherapy, hormone therapy and biological therapy. Examples of biological therapies are vaccines, monoclonal antibodies, anti-angiogenics and cancer growth blockers. It is not always clear which treatment to prefer and the preferences can change very quickly with the development of the new techniques. Physicians often prescribe combined techniques for optimization of the treatment. In an attempt to systematically determine the fraction of breast patients that should be treated with different techniques, Delaney et al. concluded that 87% of the patients would benefit from post surgery radiotherapy, 34% would benefit from chemotherapy and 68% from hormonal therapy[4]. For prostate cancer there are three main treatment alternatives: external radiotherapy, radical surgery, and brachy therapy. For symptom-free prostate cancer there is also an option to apply “watchful waiting”. In many cases the decision on treatment can

be done by the patient based on information received by the physician or through other means. There are no consistent results from the patient preference studies that has been performed [5], just as there are no conclusive clinical evidence in favor for any of the alternatives [6]. The expected survival for prostate patients is long and it is therefore necessary to have long patient follow up times in clinical evaluations of new techniques [7]. The treatment technique could therefore be obsolete before it is properly evaluated [8]. For head and neck cancer radiotherapy is often a part of the treatment [9, 10], and new treatment techniques have made a large impact on the treatments of the geometrically complex head and neck region [11]. The curative prostate, breast and head and neck treatments together with the general palliative treatments accounts for the vast majority of cases for external radiotherapy. Radiotherapy is a cost effective treatment technique which is a part of the recommended treatment for around 50% of the cancer patients in Sweden, but accounts for less than 6% of total costs for cancer care [12].

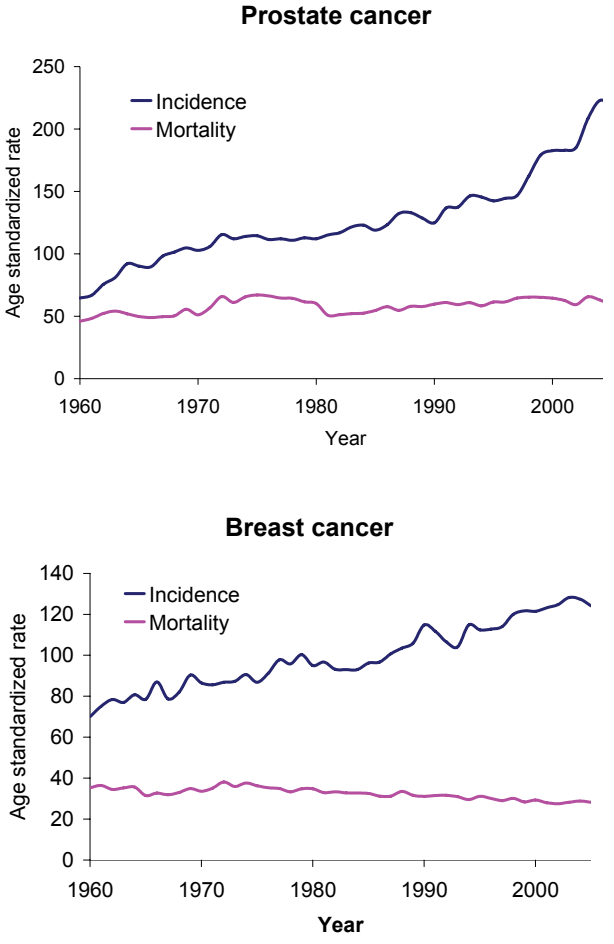

Figure 3 Incident rate and mortality rate for prostate and breast cancer in Sweden over the last 50 years. The rates are age standardized and is per 100 000 inhabitants [2].

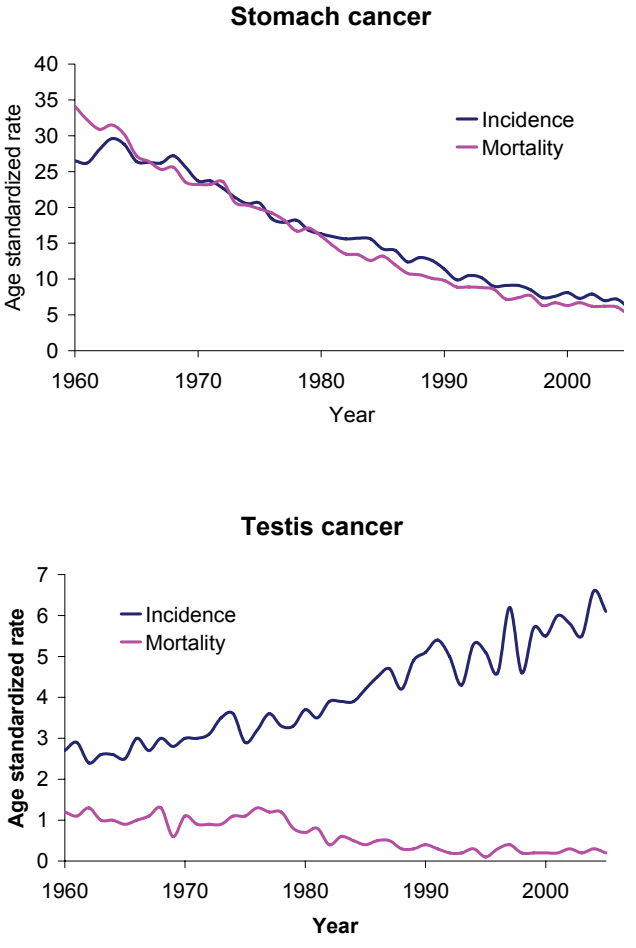

Figure 4 Incident rate and mortality rate for stomach and testis cancer in Sweden over the last 50 years. The rates are age standardized and is per 100 000 inhabitants [2].

The goal for a radiotherapy clinic is to provide the best possible treatment and care for the patients. The activities designed to reach this goal in a professional and reproducible way are often referred to in terms of Quality Assurance (QA). The QA in Swedish health care is regulated within the health and health care law which is interpreted in SOSFS 1996:24. In a summary it is stated that: *A system for treatment planning, execution, follow-up and quality development shall always be defined within each health care organization.* This means that each patient should be able to trust that the best available treatment is planned and executed in accordance with the state of the art.

Radiobiology and fractionation

An effective quality assurance strategy for radiotherapy needs to be based on knowledge about the consequences of treatment uncertainties. Radiobiological models and theories can be used to assess the connection between dosimetric uncertainty and treatment response.

Absorbed dose is a measure of energy deposition from ionizing radiation in matter and has the unit Gy (J/kg). It requires several hundreds of Gy to induce immediate cell death. At these high doses all cellular functions cease and the cell dies in interphase. These high doses are however not relevant in traditional radiotherapy. At lower doses the mechanism behind cell death in is induction of DNA damage. Ionizing radiation can damage DNA in two ways: (1) direct action occurs when a charged particle with sufficient energy interacts directly with a molecule in the DNA, and (2) indirect action is when a radical ($\bullet OH$) is produced through interaction between ionizing radiation and a water molecule. The radical interacts in a second step with a molecule in the DNA. The indirect action is the dominating effect for photon and electron radiation.

A simplified model for the cell survival probability can be created with the assumption that the risk for irreparable DNA damage to a healthy cell per dose unit is independent of the previously delivered dose, i.e.

$$\frac{dN}{dD} = -kN \qquad \textbf{(1)}$$

where N is the number of cells in a population, D is the delivered dose and k is a constant which depends on how radiation sensitive the cells are. Equation (1) has the trivial solution

$$N = N_0 \mathrm{e}^{-kND} \qquad \textbf{(2)}$$

where N_0 is the number of healthy cells when $D = 0$. The surviving fraction of the cells is often used instead of the number of healthy cells. The surviving fraction (SF) is defined as the ratio N/N_0. The simple model in equation (2) corresponds to that each single ionizing particle has a certain probability of killing a cell, i.e. there are no multiplicative effects. It has, however, been shown that the probability for cell depth per unit dose increases with increasing total dose. The commonly used linear-quadratic- or $\alpha\beta$-model takes this into account. The number of surviving cells is expressed as

$$N = N_0 e^{-D(\alpha + D\beta)} \qquad \textbf{(3)}$$

where α and β are cell property dependent parameters. The ratio α/β is commonly used as a characterization of a tissue's radiobiological properties.

Fractionation in radiotherapy means that the dose is delivered in a number of smaller parts (fractions) over a time period. The number of

live cells after a fractionated treatment with n fractions and a fraction dose d can be expressed as

$$N = N_0\left(e^{-d(\alpha+d\beta)}\right)^n = N_0 e^{-D(\alpha+d\beta)} = N_0 e^{-D\alpha\left(1+\frac{d}{\alpha/\beta}\right)} \quad \textbf{(4)}$$

Cells tolerate fractionated irradiation better than to single dose treatments. The increase in tolerance is most pronounced for cells with low α/β as seen in Figure 5.

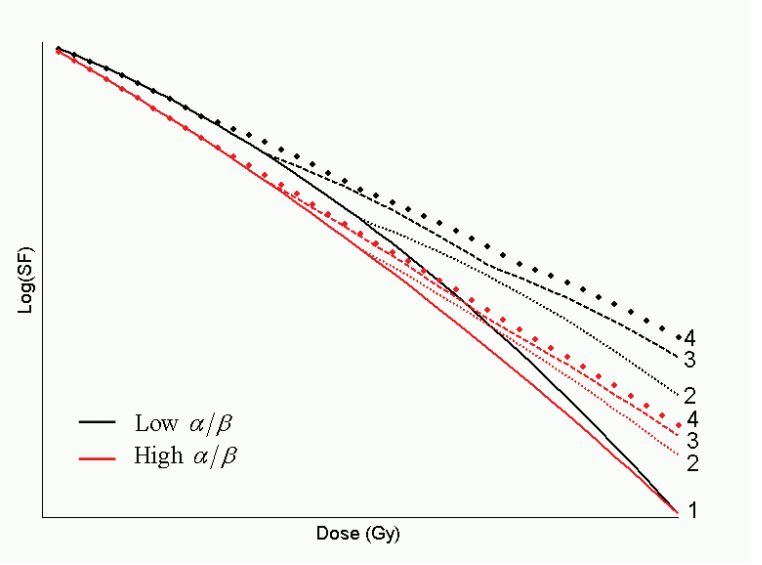

Figure 5 Illustration of the effect of delivering a fix dose in 1-4 fractions for cells of high or low α/β. The number of fractions corresponding to each line is given to the right in the figure. Cells with low α/β are spared by the fractionation to a higher degree than those with high α/β. The data is normalized in order to make the surviving fraction for both kinds of cells identical when the dose is delivered in one large fraction. (simulated data based on equation (4))

One surviving cancer cell after treatment can be enough to cause reoccurrence of the disease. The probability for controlling the disease (the Tumour Control Probability, TCP) is therefore proportional to the probability of killing all cancer cells. If the number of cancer cells from the beginning is known and the probability for killing each individual cell is known, then the probability for killing all cells can be calculated. The number of surviving cells is Poisson distributed, thus the probability for killing all cells can be written as:

$$\mathrm{TCP} \sim e^{-N_0 \mathrm{SF}} = e^{-N_0 e^{-D\alpha\left(1+d/(\alpha/\beta)\right)}} \qquad (5)$$

The tumor control probability has typically the shape of a s-curve as shown in Figure 6

The TCP model presented here is a simple but yet illustrative and serves as an illustration of the concepts. For a more complete discussion around fundamental aspects for radiobiology, see references [13, 14].

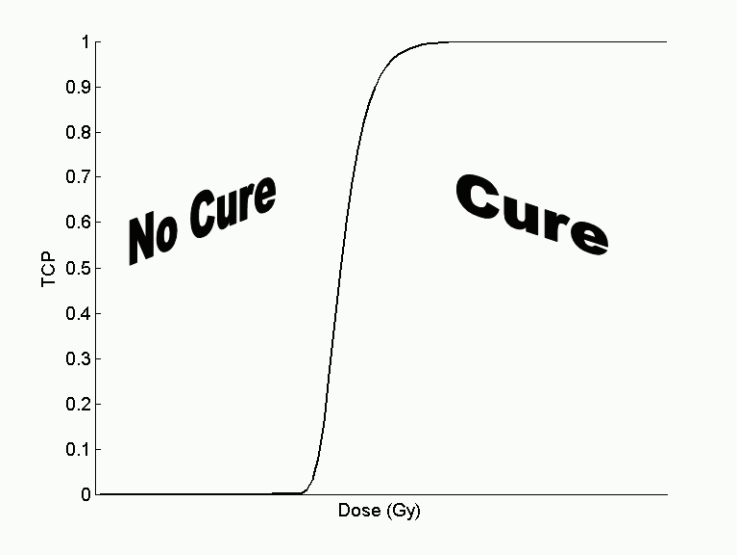

Figure 6 Illustration of a typical TCP curve. It is necessary to reach a certain relatively distinct dose level to get a reasonable probability for killing all cancer cells. (Simulated data based on equation (5))

Normal tissue is also affected by the irradiation. Radiotherapy is always a balance act between levels of harm acceptable to normal tissue and maximization of the cure probability. Normal Tissue Complication Probability (NTCP) is the equivalent to TCP for normal tissue. In practice the NTCP is complex and NTCP models must rely on extensive patient follow-ups in order to be valid [15, 16]. To maintain the simplicity in this work, it is assumed that the NTCP and TCP have similar dose dependence. The TCP combined with the NTCP can be used to form the therapeutic window, i.e. to identify the dose which balances between TCP and NTCP. Using the simplified NTCP representation as described above it is possible to define the Treatment Success Probability (TSP). The relation between TSP, TCP and NTCP is visualized in Figure 7. It should be stressed that TSP is a

purely theoretical construction which only holds a value as a symbolic representation of the therapeutic window.

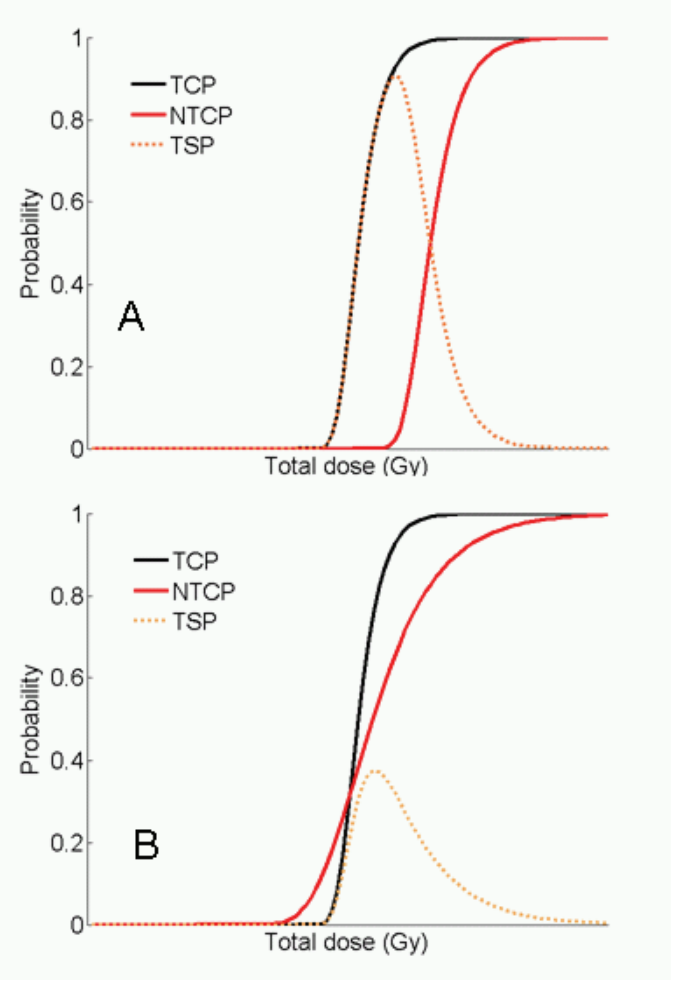

Figure 7 The relation between the probability for a successful treatment (TSP), and the TCP and NTCP for two different tissues. In A the TSP can be high with a correctly delivered dose as the TCP and NTCP is separated. In B the situation is more problematic but there is anyhow a distinct optimum dose. (Simulated data based on equation(5))

The effect of small errors in the delivered dose can be estimated using the slope of the TCP curve [17]. The parameter γ_{50} is defined as the slope of the TCP curve at the 50% level. If $\gamma_{50} = 3$ and the delivered dose is 3% lower than expected, the TCP will be reduced by approximately 9% (assuming that the optimal dose gives a TCP of 50%). Estimations of γ_{50} for different kinds of tumors are listed in Table 1.

Table 1 The γ_{50} value observed in different clinical studies and gathered in the review by Okunieff et al. [18]. In general γ_{50} tend to be higher for lower grade diagnoses, i.e. for cases with better prognosis.

Tumor	Gamma 50
Lung	1.7 – 2.17
Nasopharynx	1.67 – 32.2
Breast	0.04 – 1.55
Superglottic	0.63 – 4.1
Prostate	0.6 – 1

From a QA perspective, knowledge about the shape of the TCP and NTCP curves can be used in a consequence analysis of dosimetric uncertainties. Uncertainties in dose can be connected to increased uncertainty in treatment response, even though the relation in itself is uncertain as can be seen in Table 1. The sensitivity to dosimetric uncertainty differs between different patient groups, which can be reflected in different requirements on the dosimetric accuracy.

Quality control in radiotherapy

There are high demands on quality control in radiotherapy. Treatment errors are difficult to identify retrospectively because the effects usually appear a long time after the treatment and because the symptoms can be diffuse and be similar to problems common also after correct treatments. Errors in the dose delivery can lead to reoccurrence of the disease, reduced organ functions or in case of large overexposure even organ failures [19]. Even if an error is found, it is seldom possible to take corrective action. Therefore the QA at a radiotherapy department should be focused on preventive actions, with regular evaluation and updates of the procedures [20]. The preventive actions typically include education, maintenance and verifications. There are two kinds of dosimetric situations which should be addressed within the QA framework – large random errors (accidents) and systematic errors.

Accidents

The accidents are the spectacular mistakes which sometimes even end up in the newspapers. It is typically the large over-exposures which catch the public's attention. The listed accidents in Table 2 are in three cases caused by errors made in manual calculation or transcription of data. One accident can be blamed on lack of radiotherapy expertise and two are partly the result of hardware or software malfunction or lack of an alarm system. Noel et al. has investigated the root cause of deviations observed during in-vivo dosimetry for a large number of patients (7519) [21]. In total 79 errors were found which could be categorized based on the origin of the error. 46 were calculation errors or errors in transcription of data, 19 suspected errors were from manual entering of monitor units (MU) at the treatment unit, 7 were errors in the treatment setup (missing wedge, block etc), 3 errors each for wrong prescribed dose and erroneous data to the treatment planning system, and 1 error was due to a mechanical failure at a the

timer for a cobolt unit. The same pattern can be seen in the report from Yeung et al., where it is reported that 57% of the incidents were caused by error in data transfer and 10% from poor communication [22]. Based on these studies and on the accidents listed in Table 2, it is clear that the human factor is the cause for a large majority of the incidents and accidents in external radiotherapy. The risk for software errors should however not be neglected as illustrated in Table 3

Table 2 List of the most spectacular known external radiotherapy accidents during the 21th century.

Where	When	What
Epinal, France	2001-2006	Overuse or portal imaging. 400 patients overexposed by approximately 8%.
Glasgow, Scotland, United Kingdom	2006	Error in manual dose calculation step. One death. [23]
Epinal, France	2004-2005	Confusion when moving from physical wedges to dynamic wedges. Several severe injuries and deaths [19, 24]
Lyon, France	2004	One death. Unit confusion, field size.
Bialystok Oncology Center, Poland	2001	Accelerator failure. The dose monitor was not functioning correctly after a loss of power. Several severe injuries [25]
Instituto Oncologico Nacional, Panama City, Panama	2000 – 2001	Error in usage of TPS. 5 deaths and totally 28 injuries. [26]

Table 3 List of reported bugs from the TPS vendors collected from the FDA MAUDE database for the time period 2004-2008. The companies are not obligated to report all problems, and different companies have different policies regarding the reporting. The presented list of identified bugs are therefore far from complete and is perhaps not even representative.

Year	Report Number	Problem
2007	8043933-2007-00003	The MLC is not taken correctly into consideration under certain circumstances.
2006	MW1039971	Calculation error for physical wedges
2006	1937649-2006-00004	Physical wedge included in dose calculations but not in RTPlan exported to OIS system
2006	1937649-2006-00003	Position of X-jaw was ignored for Siemens accelerators, i.e. the field size was too large in the calculations
2006	9617016-2006-00001	MU calculations up to 5 times wrong.
2005	1937649-2005-00003	Dose calculations not removed or updated when changing treatment unit within the TPS
2005	1937649-2005-00001	Underestimation of the dose in the penumbra under specific circumstances for Siemens accelerators. Leads to cold spots in IMRT plans.
2004	1937649-2004-00004	Calculation error for Varian EDW when the central axis is blocked

The study of Noel et al. is from 1995 and the Yeung study is based on data collected from 1992 to 2002. Since then there has been an evolution of the radiotherapy workflow towards more digital data transfer, usage of oncology information systems to keep track of the treatments, and a higher fraction of treatments planned within a treatment planning system. One can therefore state that the overall safety of radiotherapy has improved.

The International Commission for Radiation Protection (ICRP) has categorized reported accidents to find adequate means for prevention in the future [27], see Table 4. It is concluded in the report that many of these accidents could have been prevented through independent verification of the TPS and with systematic use of in-vivo dosimetry.

Table 4 46 accidents/incidents reported for external radiotherapy as categorized by ICRP [27]. In the ICRP report it is stated that the category "Treatment setup and delivery" is most probably under-populated compared to reality.

TYPE	#
Equipment problem	3
Maintenance	3
Calibration of beams	14
Treatment planning and dose calc	13
Simulation	4
Treatment setup and delivery	9

Systematic errors

Dose errors of a few percent affect the individual patient's prognosis to some degree [17], and can have a large effect on a cohort of patients. Dosimetric uncertainty is especially problematic in clinical trials where it necessitates an increase of the number of included patients [28]. Table 5 provides a schematic overview of the factors which affect the total uncertainty in the delivered dose to the patient. In the investigations administered by EQUAL-ESTRO in the end of the nineties [29] it is indicated that around 3% of the dose deliveries to standardized geometries are associated with an error above 5%. In patient geometries the dose errors can be expected to be larger due to additional inaccuracies in inhomogeneous media. Dvorak et al. have compared calculations and measurements in a lung phantom and found calculation inaccuracies of up to 3% for a point kernel model and up to 6% for a pencil kernel model [30]. Knöös et al. shows with use of Monte Carlo simulations that pencil kernel calculations in lung can cause an error of up to 14% for high energy beams [31].

The dose uncertainty in radiotherapy is to a large extent an inherent uncertainty in the methods and not a consequence of human mistakes or malfunction of the equipment. The total dose uncertainty excluding the uncertainty in the dose calculation has been estimated by Andreo to 4.1% [32], which is in agreement with the estimation by ICRP [27], see Table 5. The total uncertainty can be expected to be in the region of 5 – 6 % for a typical treatment fraction.

Table 5 The components of the relative standard uncertainty in dose delivery (from ICRP report 86 [27]). The column "Total" gives the estimated total uncertainty, while the column "Clinical comparison" gives the uncertainty which is possible to observe through comparison between different clinics. *Uncertainty in protocols **Uncertainty in water to tissue transfer

	Total (%)	Clinical comparison (%)
Absolute dose determination	2.2	1*
Relative dosimetry	2.1	2.1
Dose delivery	3,4	3,4
Total uncertainty excluding dose calculation	**4.6**	**4.2**
Dose calculation	3,7	3,2**
Total uncertainty	**5.9**	**5.1**

The different uncertainties presented in Table 5 can be further categorized based on stochastical properties. The uncertainty in the absolute dose determination, i.e. the calibration of the accelerators, is both caused by inaccuracies in the calibration protocols and uncertainties in the actual measurements at the clinic. As a large part of the radiotherapy community uses the same calibration protocols, some uncertainties are systematic for the entire community. The uncertainties in the absolute dose measurements introduce errors which are systematic for specific treatment units or clinics, but appear

random when comparing different treatment units or clinics. The uncertainties in the dose calculations are related both to the algorithms used and to the quality of the commissioning data used (relative dosimetry). The errors can be different from patient to patient, but for a specific patient the uncertainty is systematic. The dose delivery uncertainty consists of instability in the accelerator output and patient positioning. For the individual patient at least a portion of this uncertainty can be seen as random from fraction to fraction, and thus has the tendency of evening out over the full treatment period. For the individual patient it can therefore be argued that the dose calculation uncertainty is in general the largest contributor to the total target dose uncertainty.

Clinical Workflow

The whole radiotherapy process starting from patient referral to completion of the treatment consists of many steps and involves staff of several professions. A schematic overview of the typical workflow and the relations between processes and common QC methods is presented in Figure 8. The first step is to create the patient fixation (1,Figure 8). The fixation is made to increase the reproducibility of the patient position. A 3D image reconstruction of the patient anatomy is then obtained by scanning the patient, in the fixated treatment position, with CT, MR, or Pet in any combination (2,Figure 8). The images are used to plan the treatment. A physician outlines the tumor and the volume that should be treated (3,Figure 8). This volume is called the target and is defined in 3D together with the organs at risk, typically on the CT image set. The delineated structures together with the prescribed target dose and dose restrictions for the risk organs (4,Figure 8) are used by the treatment planner to find the optimal treatment angles and to shape the treatment beams (5,Figure 8). The patient anatomy combined with the individual treatment plan is the basis for the calculation of the amount of radiation that needed to reach the prescribed dose. The design of the accelerator (7, Figure 8)

together with the flexibility of the treatment planning system sets the boundaries for the dose distributions that are achievable. The treatment plan is typically sent to an oncology information system (6, Figure 8) that handles all the monitoring of the treatment and the contact with the treatment unit. At treatment (8, Figure 8) the patient is positioned in the accelerator coordinate system, as defined during treatment planning. The quality of the treatment delivery depends on two independent processes; the positioning of the patient and the delivery of the radiation.

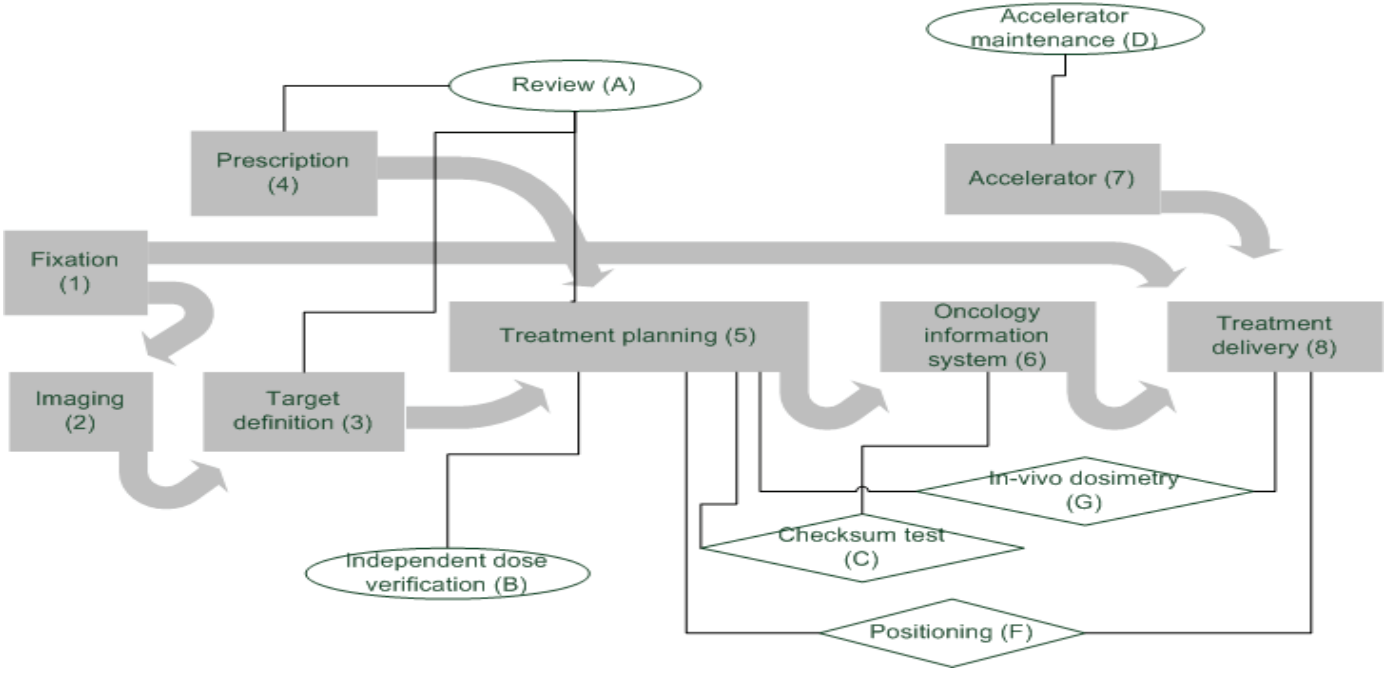

Figure 8 Overview of a generalized radiotherapy workflow and the common QC methods used. The rectangles represent workflow steps or hardware. The parallelograms represent QC procedures which compare data or output from one or several workflow steps to an expected value derived at a previous step. The ellipsoids represent QA procedures which aim at verifying the consistency of a single workflow step or hardware.

Quality control procedures

The verification procedures associated with the workflow in Figure 8 can be divided into a plan verification part (A, B) and a delivery verification part (C, D, E, F, G). The treatment plan verification answers the question: *Is this treatment plan made in accordance with the state of the art for a patient with this diagnosis?* While the delivery verification answers the question: *Are we delivering the treatment in accordance with the approved treatment plan?*

Plan verification

The delineation of the target volumes has been shown to vary dramatically between different physicians and clinics [33-35]. This is not easy to handle as there are no objective golden standard for how targets should be delineated. A system with systematic reviews of the outlined volumes can be used to achieve a standardization of the delineation within a clinic (A, Figure 8). The inter-clinic variation is problematic in clinical trials and is usually dealt with through an extensive specification of the delineation procedure to be used within the specific trial. Also, there is a development towards algorithm assistance in the target delineation. One suggestion has been to create anatomical templates which are applied to the individual patient with none rigid registration [36]. Another confounder in comparisons between clinics and in clinical trials is the different algorithms used in different TPS for creating margins around the outlined volumes. It has been shown that the resulting margins can differ significantly [37].

The treatment planning is performed in a treatment planning system. There are a handful of systems that dominate the market. Each system has its own characteristics in terms of optimization and dose calculation algorithms. For IMRT treatments large variations in plan characteristics, have been reported between clinics [38]. The inter-planner variation has been shown to be small for conventional treatments [39], while the treatment technique and equipment can

vary significantly between clinics and countries. This is exemplified by Vu et al. [40] with data describing the a large variation in the usage of bolus at radiotherapy for mastectomy patients in different parts of the world.

The QC of the treatment planning is often a review by the medically responsible physicians. The planning design can be harmonized within a clinic while the inter-clinic variations which confound clinical trials are difficult to deal with, particularly for differences caused by use of different treatment planning systems.

Independent dose calculations (IDC) (often referred to as "Independent monitor unit verification") are used to verify the dose calculation [65-67] (B, Figure 8). Traditionally the dose calculation has been performed manually and an independent check was used to find errors introduced by the human factor [41, 42]. The evolution in modern radiotherapy is going towards less manual handling of treatment parameters and manual dose calculations are becoming rare. The purpose of, as well as the demands on, the independent verification of the dose has therefore changed. Now the independent verification is primarily used to find errors in the dose calculations from the TPS. These errors can be expected to occur seldom which makes it extra important to create an efficient workflow. The digitalization of the radiotherapy clinics allows the use of digital data transfer of the treatment parameters from the TPS to the independent system, for example through DICOM RTPlan [43, 44] or through use MLC log files [45, 46].

Delivery verification

The intention of the checksum test (C, Figure 8) is to verify that the treatment parameters which are sent to the treatment unit are consistent with the approved plan. This kind of verification will in the future most probably be integrated into a complete oncology information solution with a closer connection between the treatment planning system and the treatment delivery units. A related verification is the retrospective integrity checks described by Burman et al [46], where log files of actual collimator positions recorded during treatment are compared to the content of the approved treatment plan.

Accelerator maintenance (D, Figure 8) is often divided into different categories which are performed with different time intervals. The goal is ensure the conformance of accelerator output and the calculations in the TPS.

Pre-treatment measurements (E, Figure 8) are a common verification technique for IMRT. The verifications can be divided into pre-treatment fluence verification and pre-treatment dose verification. Fluence verification compares the fluence measured with film, EPID or a matrix detector with the result predicted by the treatment planning system [47, 48]. Patient specific data are used, i.e. the same treatment settings are used during the verification as during treatment. Most commonly the comparison is made in the fluence regime but deviations can be recalculated to dose to the patient as done by van Elmpt et al [49]. Dose verifications are done by comparing calculations and measurements of the dose in a phantom irradiated in accordance with a specific treatment plan. This procedure checks both the dose calculation and the treatment unit behavior, i.e. redundant with (B, C, and D, Figure 8). In cases where it is deemed uncertain if the treatment unit can handle a specific treatment plan the pre-treatment measurements are necessary. In an evaluation by van Zijtveld et al.

[50] 270 pre-treatment verifications using EPID was analyzed. Large deviations were found for 4 patients, of which 3 were due to MLC malfunction, and in 1 case the wrong treatment plan was used.

The positioning of the patient at the treatment unit aim at spatially place the treatment origin in same position as assumed in the treatment plan (F, Figure 8). This can be achieved through different means. The traditional method to attain positioning reproducibility is to use skin marks together with room lasers. Head&Neck patients are often immobilized with thermoplastic masks. Hong et al [51] reported an average positioning error of 6mm when using thermoplastic immobilization and room laser setup. This is in agreement with the results from the review by Hunkmans et al [52]. Alternative positioning methods for Head&Neck patients are portal imaging, cone-beam CT [53] or use of optical systems. The positioning uncertainty in the pelvic region appears to be slightly larger compared to Head&Neck, and there are studies which show that the uncertainty for breast patients are significantly larger than for Head&Neck [52]. The general tendency in patient positioning is towards more frequent patient imaging for online position adjustment at the treatment session.

In-vivo dosimetry (G, Figure 8) spans over a wide range of different techniques with different ambitions. The common denominator is that measurements performed during treatment are compared retrospectively with an expected dose based on the treatment plan. In the review by Essers and Mijnheer [54], distinction is made between in-vivo measurement at every fraction, and in-vivo measurement at the beginning of the treatment series. The beginning of the treatment approach aims at finding systematic errors in the treatment, i.e. deviations from the plan. The every fraction approach does in addition aim at detection of day to day variation of the accelerator performance or patient position. In the later years several publications has dealt with the possibility to use exit dosimetry to reconstruct the

dose distribution that is actually delivered to the patient to enable correction of eventual discrepancies from the plans at the next fraction [55, 56]. The clinically most common technique is still to place diodes or TLD's within the treatment field, and to compare the reading with a calculated expected value. For TLD's high accuracy relies on well established routines and is also a time demanding technique. For diodes a number of corrections needs be applied to reach a high accuracy [54, 57, 58] and these procedures can also be demanding from a workload perspective. In Sweden the legislation require use of in-vivo dosimetry at least at the beginning of each treatment series or for every new beam that is to be delivered [59]. This kind on legislation are not present in for example France or Britain but has been discussed in the light of the accidents listed in Table 2 [60].

Independent dose calculations in the QC strategy

In the present work a verification/QC strategy feasible for implementation at a radiotherapy department is presented. A central part in the proposed strategy is a systematic use of dedicated IDC software. The fundament for this proposal is the hypothesis that an IDC is an effective tool both for identification of large random errors and detection of specific types of systematic errors.

In the publications Paper I-IV a model (algorithm) for dose calculations is described and evaluated. The model is designed to yield high accuracy with a just a very small amount of input data. In addition a method for estimating the residual calculation errors is presented.

QC Strategy

The ultimate quality objective in radiotherapy is to maximize the probability for patient cure while minimizing the treatment complications. To achieve this goal, the treatment should be delivered in accordance with the state of the art. Secondary objectives are to fulfill the boundary conditions from legislation and local policies. A competing quality goal, in most clinics, is the demands on efficiency, i.e. to keep the costs per treatment low. The means to achieve the objectives and the goals are: *Quality Assurance* (QA) and *Quality Control (QC)*. Quality control involve the procedures which are designed to verify the outcomes of a full or sub process, i.e. the different verification methods exemplified in Figure 8. Quality assurance is defined as the activities performed to assure that the process, in this case the treatment process, is implemented in an adequate way, which fulfills the quality objectives and the quality goals. A part of the QA activities is to define how extensive the QC strategy needs to be to fulfill the demands from legislation, policies, and to maintain a high patient safety standard. These demands should be fulfilled without overloading the organization or increasing the

costs to unreasonable levels. An in depth analysis of the risk scenarios connected to the radiotherapy workflow should be the basis for the QC strategy, as stressed by Fraass [61], Huq et al [62], and Rath [63]. The risk analysis is followed by the implementation of the QC, and continuous reviews of the procedures and processes [20].

Two technical evolutions have made a major impact on the QC procedures over the last years. First the digitalization and automatization of the information transfer and calculations which drastically reduce the risk for errors caused by the human factor which has been the most common root for incidents in the past [21]. Secondly the introduction of IMRT has driven the development towards more advanced verifications. The tendency is often to strive towards an as complete verification incorporated in a single procedure as possible. This can be achieved by advanced in-vivo dosimetry or pre-treatment measurements. This kind of verification is denoted “Condensed check” in this work, i.e. the verifications of a set of independent sub processes condensed into one procedure. An independent verification of a single sub process is denoted “Diversified check”. The different philosophies behind diversified and condensed checks are illustrated in Figure 9 and Figure 10.

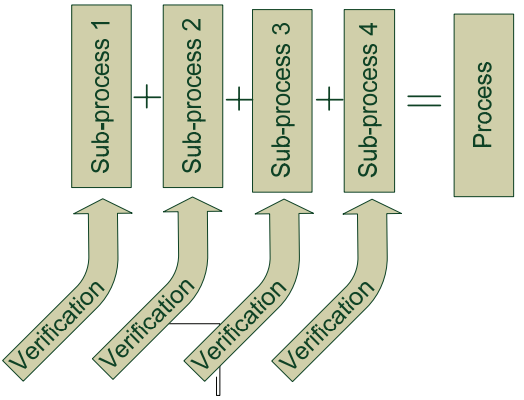

Figure 9 Diversified checks verify each sub process individually. The benefit is that it in general is easier to verify smaller and less complex systems.

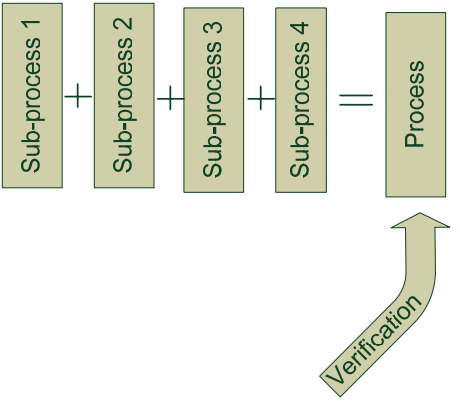

Figure 10 With a condensed check the outcome from the complete process is verified. The benefit of this concept is that eventual unpredictable interactions between the sub-processes are possible to catch.

There are numerous recommendations, standards and regulations which serve as a basis for the QA/QC at a radiotherapy department. At the end it is however necessary that each department creates its own QC strategy, designed for optimal usages of the local resources. As previously mentioned the QC strategy should be based on an analysis of where the hazards in the workflow are. What can go wrong? How

often does it occur? What are the consequences? This analysis is the basis for the design of the QC procedures. It is, however, not a trivial task to identify the potentially problematic parts of the workflow. Especially new treatment techniques or procedures can be troublesome where the department lacks experience. In these cases it can be a good idea to implement a patient-specific condensed check which verifies the output from the accelerator as close to real treatment conditions as possible. The idea with the condensed check is basically to help identifying safety issues with the new technique or procedure. For long term QC of established techniques the condensed checks can be inefficient as argued by Thomandsen [64]. If problems from a specific part of the workflow are frequently detected with the condensed technique, the resources are better spent if focused directly on the problematic area with a diversified check. Also if problems are never or very rarely detected the resources are for natural reasons better spent elsewhere. Condensed checks are effective when it is judged that errors can be introduced through unexpected interactions between sub-processes or when the sub-processes are not clearly identified. This should only be the case for new treatment techniques or procedures. The principal can be exemplified with the previously mentioned study be van Zijtveld et al. [50], where 270 IMRT plans was analyzed using pre-treatment verifications with EPID. Recall that 3 of the 4 found errors were due to MLC malfunction, and in the last 1 case a wrong treatment plan was used. This study shows that there can be a need for a review of the QC procedures at the department. The first observation one can make is that none of the 4 problems found origins in an IMRT specific procedure, and all 4 can have a large impact also on conventional treatments. A second observation is that the pre-treatment fluence measurements with EPID can detect both MLC and plan export problems but is not the most efficient method. A logical step would therefore be to put more effort into validation of the MLC, perhaps as

a part of a daily QC procedure for the treatment unit. Introducing a procedure for verification of the plan id prior to treatment would also be an important QC step. Pre-treatment measurements using EPID can still be a part of the QC strategy, but should be seen as a verification of the diversified checks rather than a verification of the treatments.

Besides the efficiency argument held against condensed checks for established treatment techniques, one can argue that condensed check suffers from an inherent resolution problem. Each sub-process in the radiotherapy workflow adds additional uncertainty, which means that the uncertainty for the complete treatment chain is both large and complex which complicates the interpretation of observed deviations. It is of course important to be aware of the uncertainties for the complete process, but the improvements will be made on the sub-process level.

In Table 6 a QC strategy is outlined. The example is based on diversified checks where the integrity of the output from each sub process is checked independently. Only the final verification of the treatment with a diode measurement condenses the results from all the sub processes in one single check. As the focus of the QC strategy is on diversified checks, one can assume a low frequency of errors at delivery. The purpose of the in-vivo dosimetry is then to detect large errors with a high efficiency and effectiveness. This is achieved using as basic input data combined with a wide acceptance interval.

There are three main origins for dose calculation errors. There can be bugs, algorithm shortcomings or errors in the beam characterization. The implementation, testing and maintenance of modern treatment planning systems are highly regulated. The frequency of bugs and errors in the sensitive parts of the systems can therefore be assumed to be low, but the consequences can still be large. The situations when bugs are involved are unpredictable. It is therefore not possible for an individual clinic to perform a complete testing of the system from a bug perspective. IDC is however an effective tool for finding this kind of errors as long as the implementation is fully independent. Algorithm shortcomings are often widely known and documented, for example the problems connected with pencil beam algorithms in low density areas [31]. Differences in algorithm performance can cause severe problems in comparisons involving different clinics or treatment planning systems, for example in clinical trials. An IDC which has been designed to yield a high accuracy and is based on a modeling of the physics, can serve as a base line in such comparisons. High accuracy is also a demand from an efficiency point of view as will be discussed in the Action limits section. Beam characterization errors can have different characteristics. In most cases these errors should be easy to detect using a set of standardized measurements [67]. This is however time consuming and the test may still not be complete. Many modern treatment planning system utilize model based dose calculations, where the characterization measurements are used to determine more basic parameters. Model based dose calculation algorithms have the benefit of being flexible, but with the drawback that errors in characterization measurements can result in unexpected calculation errors. Therefore a patient specific IDC is well suited for commissioning verification. To avoid undetected commissioning errors in the IDC and to simplify the commissioning procedure, the algorithms should be based on a minimum of measurements.

Table 6 Dosimetric quality control strategy for external radiotherapy

Process	Input	Control measures	Procedure	Output	Control measures
Prescription	Diagnosis	Review	Decide treatment area, fractionation, etc (Physician)	Prescription	Review
	Treatment record	Certified system			
Fixation	Patient	ID-Check	Create fixation (Therapist/physician)	Fixation	Reproducibility verification in sensitive cases
	Prescription	Review			
Imaging	Patient	ID-Check	The patient is imaged with one or several imaging modalities	Images	
	Imaging modality	Regular maintenance and checks			
Target delineation	Images		The physician outlines the target	Target	Review
	Diagnosis	Review			
Treatment planning	Images		A treatment is designed by a treatment planner	Treatment plan, typically in form of a DICOM RTPlan	Review
	Target	Review		Patient positioning data	
	Prescription	Review			

	Treatment planning system	Certified software			
Dose calculation	DICOM RT Plan		Sub part of the treatment planning process. Internally handled by the TPS	Monitor Units for all fields/segments	Independent dose calculation
	Algorithms	Certified software			
Information transfer/Data integrity	DICOM RT plan		Treatment data are transferred to treatment unit/Oncology information system	DICOM RT plan	Checksum test
	Positioning data			Positioning data	
Patient positioning	Fixation		The therapists positions the patient in the treatment room coordinates	Patient in position	The position is verified with EPID, Surface imaging or Cone beam imaging
	Positioning data				
	Patient	ID Check			
Treatment delivery	Patient in position	Visual Surveillance on monitor	The treatment is started and monitored by the therapists	Treatment record	In-vivo dosimetry with diodes for first fraction. Expected dose based on the prescribed dose and the treatment plan.
	Treatment unit	Regular maintenance, Daily / weekly / yearly checks.			
	DICOM RT plan	Checksum test at every fraction			

Clinical implementation of IDC

A QC procedure should ideally comply with three basic demands

1. Robust, i.e. it should be trustworthy
2. General , i.e. it should always be applicable for different techniques
3. Simple, i.e. it should not be time consuming or complicated for the staff

The two first demands are related to the IDC tool and basically states that the IDC should find all errors in the TPS calculations, and that the IDC should be applicable for all different treatment techniques with equal accuracy, i.e. there should be no need to make distinctions between different treatment techniques in the routines. From a radiobiology point of view there is no difference in the demands on the dosimetric accuracy between different treatment techniques. Recommendations to use a wider acceptance interval for the deviation between the TPS and IDC for IMRT compared to conventional treatments are based on a workload consideration and not on the clinical relevance. The third demand, simplicity, is important as the frequency of found errors can be expected to be low. A complicated or time consuming verification procedure should therefore be avoided to be able to maintain the long term focus among the staff.

Action limits

The main traditional purpose of an IDC is to catch cases when the primary dose calculation fails. The concept is simply to compare the two calculation results, either the number of MU for a specified dose or the dose, or the dose with a specified number of MU. If the deviation (δ) between the TPS calculation and the IDC is large it is an

indication that one of the calculations has failed and further investigation is needed. As all algorithms for dose calculations has an inherent uncertainty there will always be a difference between the two calculations. An example of how the distribution of deviations can be is given in Figure 11. In order to establish an objective procedure for the verification of the calculated dose each clinic need to formulate the criteria for when the observed deviation between the TPS calculation and the IDC should trigger a further investigation. The deviation interval which is acceptable is called the acceptance interval, defined through the action limits (AL_+, AL_-). A deviation outside the action limits should be investigated further.

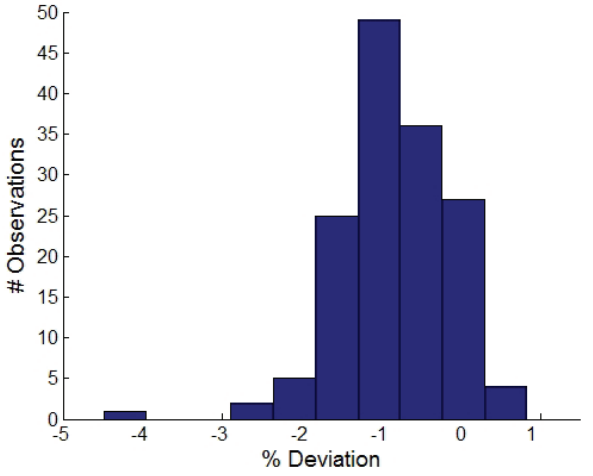

Figure 11 Distribution of deviations in calculated dose between the IDC EqualDose© and the TPS MasterPlan© for IMRT treatment in Umeå. The dose is compared in one selected point for each treatment. The point was chosen in a high dose region and not too close to dose gradients.

It is natural to base the determination of the acceptance interval for the deviation (δ) between the TPS calculation and the IDC on a clinical relevance consideration. There is no meaning to investigate

potential calculation errors which are small and have no clinical relevance for the patient. On the other hand, an investigation should always be performed if the deviation can be clinically relevant.

In addition to the standard prescribed dose D_{P} which is used for each specific diagnosis, one can form a tolerance interval for the true delivered dose (D_{T}). The tolerance interval is defined through an upper and a lower dose level $\mathrm{TL}_{\Delta\pm}$ around the prescribed dose (see

Figure **12**). Note that the tolerance interval does not need to be symmetric around the prescribed dose. In cases where the probability distribution for the TSP is asymmetric around its maximum (Figure 7B) it is natural to use an asymmetric tolerance interval.

The IDC is an estimation of D_{T}, ideally unbiased but always connected to an uncertainty. The dose calculation uncertainty can be expressed through the standard deviation σ. If σ is known it is trivial to calculate the risk that D_{T} is outside the tolerance interval. This risk, indicated in

Figure **12** as P_{Error}, can with normality assumption never be zero. To be able to calculate the action limits for a deviation between the TPS calculation and the IDC, an acceptable risk α needs to be defined. When $P_{\mathrm{Error}} > \alpha$ further investigations should be performed. It should be noted that P_{Error} and α are, despite their simple definition, not possible to interpret as real probabilities when the predictive power of the TPS calculation is neglected. This is natural as the verification procedure should be totally independent of the TPS result. No assumptions regarding the accuracy of the TPS calculation should therefore be done in the procedure.

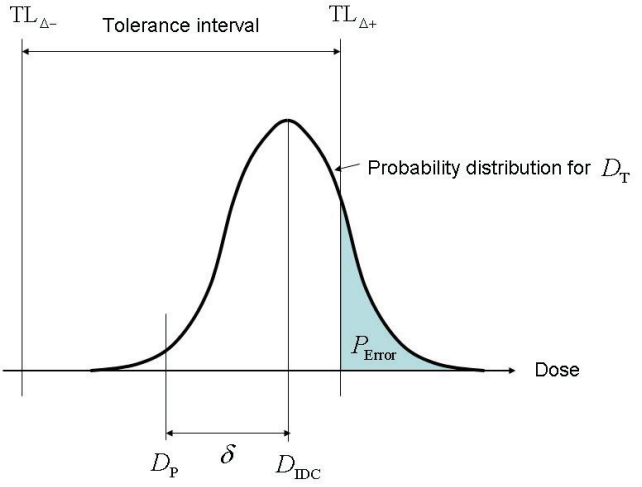

Figure 12 When the uncertainty in the IDC is known the probability distribution for the true dose (D_T) can be formed. The probability that the dose true dose is outside the tolerance interval (P_{Error}) depends on the probability distribution for D_T .

One of the implications of the described concept is that a reduction of the IDC uncertainty σ makes it possible to allow a wider acceptance interval for δ and vice versa. This means that the number of false positives and therefore also the workload increase fast with increasing uncertainty in the independent calculations. It is therefore of importance to use IDC's with small and predictable uncertainties. This is illustrated by the result of a few simple calculations presented in Table 7.

Table 7 Examples of the relation between the Tolerance Limits (TL), the uncertainty in the IDC calculation (σ) and the Action Limit (AL) for the deviation between the TPS calculation and IDC (δ). To maintain a high efficiency, i.e. keeping the false alarm frequency low, the uncertainty in the IDC needs to be low. The action limits are calculated to fulfil the criteria $P_{\text{Error}} < \alpha$.

$TL_{\Delta\pm}$	σ	α	$AL_{\delta\pm}$
6%	1%	5%	$\approx \pm 4\%$
6%	2%	5%	$\approx \pm 2\%$
6%	3%	5%	**Always needs to check**
8%	2%	5%	$\approx \pm 4\%$
12%	**2%**	**5%**	$\approx \pm 8\%$

Statistical analysis and inter-clinic comparisons

As stated above, an IDC can be used as a baseline for dose calculation comparisons between clinics. The comparisons can be of value both in clinical trials and as a regular QC procedure at individual clinics. The calculation results from the TPS and from the IDC can be stored in both a global database and a local database at the clinic. The data in the global database can be fully anonymous both with respect to patient and clinic (Figure 13). Through comparisons between the databases, each clinic can judge if their calculation results are reasonable in the light of the results from the rest of the community (Figure 14).

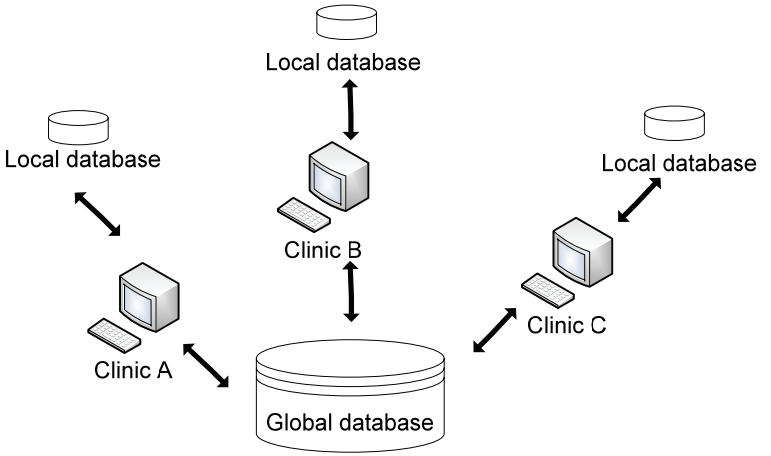

Figure 13 The database architecture with a global anonymous database and a local database at each clinic makes it possible for each clinic to see their own data in relation to the state of the art, but prevents identification of data for other clinics.

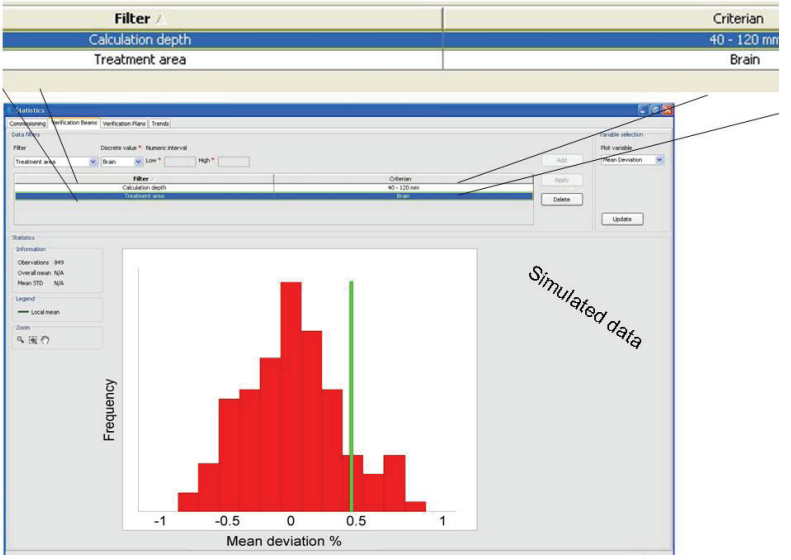

Figure 14 Screen shot from EqualDose© with simulated data. Deviations scored for brain treatment beams with a calculation depth between 40 and 120 mm are gathered from both the global and the local database. The data are presented as a histogram of mean deviations per clinic. The mean deviation for the own clinic is presented with the high light bar. If the mean deviation for the own clinic appears to be untypical it should trigger an investigation.

The usefulness of the database solution sketched in Figure 13 is highly dependent on the quality of the stored data. It should be noted that it is necessary to normalize the calculations in a standardized fashion, i.e. with the IDC, to be able to compare the dose calculations from different clinics. The stored deviations can have the form

$$\delta = \frac{D_{\mathrm{TPS}} - D_{\mathrm{IDC}}}{D_{\mathrm{IDC}}} = \frac{D_{\mathrm{TPS}}}{D_{\mathrm{IDC}}} - 1 \qquad (6)$$

where D_{TPS} is the dose calculated by the treatment planning system. The prescribed dose (D_{p}) and D_{TPS} are identical for the dose specification point. Equation (6) can symbolically be expanded into

$$\delta = \frac{D_{\mathrm{T}}\left(\mathrm{A};\mathrm{P}\right)\cdot F_{\mathrm{TPS}}^{\mathrm{B.M.}}\left(\mathrm{A}\right)\cdot F_{\mathrm{TPS}}^{\mathrm{Algo}}\left(\mathrm{A};\mathrm{P}\right)}{D_{\mathrm{T}}\left(\mathrm{A};\mathrm{P}\right)\cdot F_{\mathrm{IDC}}^{\mathrm{B.M.}}\left(\mathrm{A}\right)\cdot F_{\mathrm{IDC}}^{\mathrm{Algo}}\left(\mathrm{A};\mathrm{P}\right)} - 1 \qquad \textbf{(7)}$$

where D_{TPS} has been factorized into the true dose (D_{T}), $F_{\mathrm{TPS}}^{\mathrm{B.M.}}$ which corrects for all beam model approximations and commissioning errors, and $F_{\mathrm{TPS}}^{\mathrm{Algo}}$ which accounts for any algorithm dependence. The factorization of D_{ICD} is equivalent. The parameter A represents the treatment beam, i.e. the collimator settings, gantry angle, wedges, etc; and the parameter P represents the patient. Ideally both $F^{\mathrm{B.M.}}$ and F^{Algo} should be close to unity with only a weak dependence on A and P, both for the TPS and the IDC. If the IDC is assumed to be ideal, i.e. $F_{\mathrm{IDC}}^{\mathrm{B.M.}} = F_{\mathrm{IDC}}^{\mathrm{Algo}} \equiv 1$ then the deviation stored in the database is simply the calculation error for the treatment planning system without any physical A and P dependence. The value of the stored deviations are reduced if the errors in the IDC calculation are dominating and especially if they are strongly dependent on A and P. This can be exemplified with the situation where the IDC does not take the patient geometry into consideration at all. This can be expressed as

$$\delta = \frac{D_{\mathrm{T}}\left(\mathrm{A};\mathrm{P}\right)\cdot F_{\mathrm{TPS}}^{\mathrm{B.M.}}\left(\mathrm{A}\right)\cdot F_{\mathrm{TPS}}^{\mathrm{Algo}}\left(\mathrm{A};\mathrm{P}\right)}{D_{\mathrm{T}}\left(\mathrm{A};\mathrm{W}\right)\cdot F_{\mathrm{IDC}}^{\mathrm{B.M.}}\left(\mathrm{A}\right)\cdot F_{\mathrm{IDC}}^{\mathrm{Algo}}\left(\mathrm{A};\mathrm{W}\right)} - 1 \qquad \textbf{(8)}$$

where W indicate that the calculation is performed in a homogeneous water phantom geometry. In equation (8) it is clear that δ will be dominated by the differences in calculation geometries, and that the histograms such as in Figure 14 will be biased by the

frequency of different treatment areas at different clinics. This can be partly mitigated through the possibility to filter on treatment area, as shown in Figure 14.

The infrastructure with a global database which is accessible from individual clinics does also open the possibility to collect and share beam characterization data for the verification of the beam commissioning.

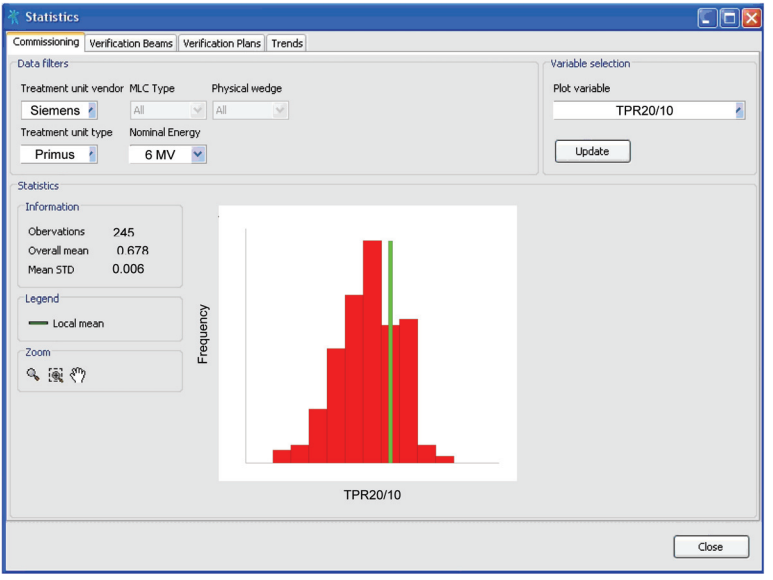

Figure 15 Screen shot from EQUAL-Dose © showing simulated TPR20/10 data for Siemens 6MV beams. The high light bar represents the measured TPR20/10 value for a local treatment unit. If the measured value for the local treatment unit deviates significantly from the common values an investigation should be initiated. The same principal can be applied for all common characterization measurements.

IDC algorithms and uncertainties

A distinction can be made between factor and model based algorithms. In a factor based model the dose per monitor unit is typically expressed as the dose to a reference point under reference conditions, corrected with a set of factors. Each factor accounts for one or several different effects, such as beam size, beam shape, depth, distance, wedges, etc. [65, 68]. The factors are typically measured or calculated through simple modeling and stored in tables. The method is intuitive and robust but lacks general applicability. It is in principal impossible to account for all different treatment design possibilities which are a part of modern radiotherapy. Therefore the model based calculation methods are dominating within treatment planning systems, and are also the best choice for an IDC tool. In a model based algorithm the commissioning measurements are used to determine a set of more fundamental physical parameters which characterize the radiation from the treatment unit [69-71]. Model based algorithms can be made fully general without the need for a large set of characterization measurements, as shown in Publication I and by Olofsson et al. for a multi source energy fluence model [70]. Even with a very limited set of characterization measurements it has been shown that it is possible to achieve adequate calculation accuracy (Publication IV and [43, 44, 72]).

In the Action limits section it is shown how the uncertainty (expected standard deviation - σ) for the IDC can be used to numerically estimate an adequate action limit for the deviation between the TPS calculation and the IDC. The calculation uncertainty is not easy to assess as it is dependent on a large variety of parameters. Jin et. al. [73, 74] models the calculation uncertainty through three assumed independent factors; the dose gradients, distance to the field edge, and distance to the central axis. The strategy in the work by Jin et. al. is to assume simple models for the uncertainty, fitting the model parameters to a training set, and then test the result on a verification

set of data. The same strategy has also been applied by Olofsson et. al. [70, 72] and publication IV, and Nyholm et. al. in publication III.

Summary of publications

The publications included in the present thesis are focused on the development and evaluation of a model for calculation of the absorbed dose in a semi-infinite water slab phantom. The required input to the model is the properties of the radiation field characterized with the beam quality index $\mathrm{TPR}_{20/10}$ and the energy fluence distribution. The energy fluence model describe by Olofsson et. al. [70] is used in publication II – IV. The development of the pencil dose deposition kernel model has been focused on high accuracy, small amount of input data (or generic input data), and predictability of the resulting calculation uncertainty. The uncertainty estimation model for the dose deposition is described in publication III and evaluated in publication IV.

Publication I

Photon pencil kernel parameterisation based on beam quality index

Nyholm, T. Olofsson, J. Ahnesjö, A. Karlsson, M. , Radiotherapy and Oncology,78(3), 347-51, 2006

In publication I a pencil kernel model previously described by Ahnesjö et. al. [75] is generalized with a parameterization of the depth dependence for the pencil kernel parameters. The derived model which consists of a total of 102 parameters, relates the beam quality index $\mathrm{TPR}_{20/10}$ to the dose deposition properties of a clinical photon beam. The model was optimized using measured data from 593 clinical beams originating from Nucletron's database of customer commissioning data [76]. Through the optimization the calculation errors on the central axis were reduced, and can be expected to be within ± 2 % at clinically relevant depths.

Both the energy fluence and the beam quality were assumed to be laterally invariant in publication I. Under this assumption the dose to a point $\mathbf{x}$ can be expressed within a radiation field A as:

$$D(x;\mathrm{A}) \sim \Psi_0 \int_{I(\mathrm{A})} \frac{p}{\rho}\left(|\mathbf{x}-\mathbf{p}|, d; \mathrm{TPR}_{20/10}\right) d^2\mathbf{p} \qquad \textbf{(9)}$$

where I is the open field which is symbolically determined by the beam settings A, d is the depth, $\frac{p}{\rho}$ is the dose deposition kernel, and Ψ_0 is the laterally invariant energy fluence.

Publication II

Modelling lateral beam quality variations in pencil kernel based photon dose calculations

Nyholm, T. Olofsson, J. Ahnesjö, A. Karlsson, M. , Physics in Medicine and Biology, 51(16), 4111-8, 2006

In publication II the expression for the dose to the point $\mathbf{x}$ in equation (9) is generalized to enable modeling of lateral variations for both the beam quality and the energy fluence. The generalization was complicated by the fact that the beam quality index $\mathrm{TPR}_{20/10}$ is defined by measurements on the central axis. However, by transforming the pencil kernel dependence to another descriptor for which off-axis softening relationships exist, i.e. the half-value-layer HVL, then the pencil kernel fluence convolution can be generalized to:

$$D(\mathbf{x},d;\mathrm{A}) \sim \int_{I(\mathrm{A})} \Psi(\mathbf{p};\mathrm{A}) \frac{p}{\rho}\left(|\mathbf{x}-\mathbf{p}|,d,\mathrm{HVL}\left(\mathbf{p},\mathrm{TPR}_{20/10}\right)\right) d^2\mathbf{p} \qquad \textbf{(10)}$$

where Ψ describes the energy fluence distribution. A generic expression for the lateral HVL over clinical beams has previously been presented by Tailor et. al. [77]. When we combined Tailor's expression with equation (10), we achieved excellent dose calculation results as shown in publication II.

Publication III

Pencil kernel correction and residual error estimation for quality-index-based dose calculations

Nyholm, T. Olofsson, J. Ahnesjö, A. Georg, D. Karlsson, M., Physics in Medicine and Biology, 51(23), 6245-62, 2006

Even after the extensive optimization of the pencil dose deposition kernels made in publication I residual errors remains. The introduction of the modeling of the lateral beam quality variations described in publication II further increases these errors, due to an increase in the scatter contribution. Using the same database of measured data as used in publication I a correction of the pencil kernel was derived and fitted with the model. The correction term $\frac{\varepsilon}{\rho}$ was applied to the pencil kernel as:

$$\frac{p}{\rho}(r,d,\mathrm{QI})_{\mathrm{Corr}} = \frac{p}{\rho}(r,d,\mathrm{QI}) + \frac{\varepsilon}{\rho}(r,d,\mathrm{QI}) \qquad (11)$$

where r is the radius and QI is the beam quality index used. The correction term $\frac{\varepsilon}{\rho}$ was expressed in terms of the observed deviations between calculations using the original model and measurements from the database as:

$$\frac{\varepsilon}{\rho}(r,d,\mathrm{QI}) = -\frac{\frac{\partial}{\partial r}\left[\bar{Q}(r,d)D_{\mathrm{C}}(r,d)\right]}{2\pi r\Psi(r)} \qquad (12)$$

where $D_{\mathrm{C}}(r,d)$ is the calculated dose for a circular field with radius r at depth d. $\bar{Q}(r,d)$ is the mean relative deviation between the calculation and measurements as a function of the radius and depth, according to:

$$\bar{Q}(r,d) = \frac{1}{N}\sum_{i=1}^{N}\frac{D_{\mathrm{C},i}(r,d) - D_{\mathrm{M},i}(r,d)}{D_{\mathrm{C},i}(r,d)} \qquad (13)$$

in which $D_{\mathrm{M}}(r,d)$ is the measured dose for the circular field.

This correction is shown to increase the accuracy of the calculations. There are however still residual errors. These are modeled through an intrinsic uncertainty in the pencil kernel and the simplification that the uncertainty for different radii are handled as being independent. The uncertainty estimation model is shown to provide reasonable results.

Publication IV

Evaluation of uncertainty predictions and dose output for model-based dose calculations for megavoltage photon beams

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Publication IV evaluates the pencil dose deposition model with corrections and uncertainty estimation as described in Publication III, combined with the model for the energy fluence distribution derived by Olofsson et. al. [70]. In total 300 measurements were performed for 10 different beam shapes on 3 different depths for 10 different clinical beams. Results showed that the errors in the calculations with the pencil kernel, i.e. the dose deposition per energy fluence, where very small (mean: 0.1%, std: 0.4%). The combined uncertainty for the full dose calculation was also very small (mean: -0.04% std: 0.47%). The results from the uncertainty estimation were more difficult to assess due to the fact that the residual errors were small and that they probably originated mainly from the measurement uncertainty.

Conclusions and future developments

The design of the QC procedures for a radiotherapy department must balance between efficiency and costs on one side and patient safety and treatment quality on the other.

Does the IDC concept provide the right balance? In the chapter “Action limits” a verification methodology aimed at large random errors was described. The direct connection between the action limits and the tolerance interval for the true dose is an objective method to focus the resources in a clinically relevant way. It is intuitive to spend extra verification efforts for patients who clinically benefit from very accurate dose delivery. The proposed action limit concept is therefore cost effective. In the section “Statistical analysis and inter-clinic comparisons” the IDC is proposed as a baseline for comparisons of dose calculation results between clinics, TPS:s, countries etc. The described database solution connected to the IDC would enable direct access to these comparisons for every clinic, and hence provide an extremely easy and cost effective solution for identification of systematic differences. In Table 8 an assessment is made of the probability that an IDC would find the TPS bugs reported over the last years. The conclusion from Table 8 is that an IDC is an effective tool for finding errors in the TPS calculation.

Table 8 The reported TPS bugs previously listed in Table 3. The probability that the bug would have been found with an IDC is judged in the column "Found with IDC"

Year	TPS Problem	Found with IDC?
2007	The MLC is not taken correctly into consideration under certain circumstances.	Always found with 2D or 3D verification.
2006	Calculation error for physical wedges	Most probably found. Lack of detailed information.
2006	Physical wedge included in dose calculations but not in RTPlan exported to OIS system	Always found
2006	Position of X-jaw was ignored for Siemens accelerators, i.e. the field size was too large in the calculations	Always found with 2D or 3D verification.
2006	MU calculations up to 5 times wrong.	Always found
2005	Dose calculations not removed or updated when changing treatment unit within the TPS	Found if significant
2005	Underestimation of the dose in the penumbra under specific circumstances for Siemens accelerators. Leads to cold spots in IMRT plans.	Found with 2D or 3D verification
2004	Calculation error for Varian EDW when the central axis is blocked	Always found.

Are verifications in discrete point enough or is a 3D verification required? In traditional radiotherapy it has often been considered to be enough to verify the dose in one single point. It is a common opinion that we with the introduction of highly complex multi segmented treatments need to take the step to 2D or 3D verification. Table 8 shows that calculation errors can be missed by point verification also in conventional radiotherapy. It is therefore important to leave the point based approach and aim at verification in either 2D or even 3D. However, the introduction of the 2D or 3D verification should be done without losing the simplicity of the procedures.

Should the patient geometry be taken into consideration by the IDC? From a database quality perspective the answer is definitely – yes, based on the discussion around equation (8). From a patient safety perspective the question is more complex. When both the IDC and the TPS calculations are performed in the same patient geometry, they are no longer fully independent. The calculation errors in following two scenarios are not detected with an IDC utilizing the same patient geometry as the TPS:

1. Inclusion of stereotactic frames in the patient outline can induce substantial calculation errors, due to the distance between the frame and the patient's outer contour. These errors are not found if the IDC use the same patient geometry information as the TPS.

2. Mistakes when the treatment plan involves volumes which are not covered by the CT study can result in underestimation of the scatter contribution. This error is not found if the IDC is based on the same CT study.

Also from the efficiency perspective usage of CT data can be problematic, if manual import is needed. The IDC tool can, however, be designed to interface with the data infrastructure at the

department, for example a direct connection to the patient database through a DICOM interface.

In the present thesis a concept for independent verification of the dose calculations in single points is presented and put in perspective. The IDC verification should not be seen as a full QC strategy but rather as a part of a larger process. When a new treatment technique with time evolves to a clinical standard routine the QC measures should be reconsidered. For a standard treatment technique where the error frequency can be expected to be low the main focus of the QC procedures should be the simplicity and accuracy. The publications included in the present thesis describe algorithms which fulfills the natural requirements which can be put on algorithms for independent dose calculations.

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