System for dose audit for external radiation therapy based on EPR dosimetry with Lithium Formate

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Abstract

Radiation therapy is an important method to treat cancer with the aim to deliver as high doses as reasonably achievable to the tumor while protecting the surrounding healthy tissue and organs at risk, OARs. Therefore, it is essential to have high accuracy in the dose delivered clinically and quality assurances are required. In the meantime, radiation therapy techniques are becoming more advanced and complex, introducing a significant risk of random and systematic errors that needs to be investigated. Hence, the need of independent dose verifications has increased. The purpose of the present work is to design and create a mailed audit system for external evaluation of the dose to water in relevant points in a phantom, including influences from the whole treatment chain, from computed tomography, CT, scanning, to contouring of structures, treatment planning and treatment delivery.

The measurements were performed using an anthropomorphic Polymethyl methacrylate, PMMA, phantom designed to be relevant for the head-and-neck region containing inserts corresponding to tumour, salivary glands and medulla made of PMMA and that are easily distinguishable from the surroundings for contouring. Inhomogeneities of both Teflon, corresponding to the spinal cord, and air were also included. Pellet shaped electron paramagnetic resonance, EPR, dosimeters made of lithium formate with a diameter of 4.5 mm and height of 5 mm were made for the measurements. The dosimeters can be placed in various positions in the different structures of the phantom using PMMA tubes and can be analyzed using a spectrometer.

In order to test the precision and accuracy of the EPR dosimetry method, measurements with three blind tests were performed simultaneously with an ionization chamber for comparison of absorbed doses. For the audit measurement, the audit phantom was CT scanned twice both with a Siemens CT scan and GE (General Electric)) CT scan for comparison of Hounsfield Units, HU, and dose distributions. The target and the OARs were contoured in the treatment planning system, TPS, (Varian, Eclipse) and a dynamic Intensity modulated radiation therapy, IMRT, treatment plan was created. The treatment plan consisted of seven coplanar 6 MV fields giving the target a dose of 5 Gy delivered with a Varian, Clinac iX accelerator. The absorbed doses to water were determined in seven locations: three points in the target, one in each parotis, one in the medulla and one in the air cavity. The absorbed doses were determined using the signal from the EPR dosimeters and were compared to the planned doses. Also, the measured and reconstructed volumes of the structures were compared.
The blind tests doses obtained from the EPR dosimeters agreed with the results obtained from the ionization chamber within 1% and are well below the calculated uncertainties (1 SD) in the EPR measurements. The absorbed doses and the dose distributions were not affected by any spread in HU and the absorbed doses had an agreement within 0.5% in comparison between the Siemens and GE CT studies. The determined doses agreed with planned doses within 4% for all the structures except the air cavity. This deviation is not covered by the calculated standard uncertainty. However, the deviation does fall within two standard deviations, corresponding to a confidence interval of 95%. Also the measured and planned volumes had an agreement within 2.5% for smaller structures and within 5% for larger structures.

Repeating the whole measurement chain with other dosimeter batches is required using two or three dosimeters in each measurement point for higher precision. A conclusion can be made that this work showed promising initial results for an audit system for evaluation of the dose to water in relevant points in a phantom, including influences from the whole treatment chain.
Table of contents

1. INTRODUCTION ........................................................................................................... 6
   1.1 Strategy .................................................................................................................... 9
   1.2 IMRT versus Conformal Radiation Therapy ............................................................. 11

2. THEORY ........................................................................................................................... 14
   2.1 Basic EPR theory .................................................................................................... 14
   2.2 Lithium formate EPR dosimetric properties .............................................................. 17

3. MATERIALS AND METHODS ....................................................................................... 21
   3.1 Phantom design ....................................................................................................... 21
   3.2 Manufacturing of dosimeter batch .......................................................................... 23
   3.3 EPR measurements and readout ............................................................................. 24
   3.4 Dosimeter batch quality control ............................................................................. 25
   3.5 Measurements ......................................................................................................... 26
      3.5.1 CT scanning, contouring, treatment planning ...................................................... 26
      3.5.2 Calibration and blind tests ................................................................................. 28
      3.5.3 Pre treatment verification ................................................................................... 31
      3.5.4 Audit measurement ......................................................................................... 32
   3.6 Data analyses and uncertainties .............................................................................. 34
      3.6.1 Organ volumes and Hounsfield units ................................................................. 34
      3.6.2 Absorbed dose to water determination ............................................................... 35
      3.6.3 Uncertainty analyses ....................................................................................... 36
4. RESULTS AND DISCUSSIONS ................................................................. 39

4.1 Dosimeter Batch Quality Control .................................................. 39

4.2 Organ volumes and Hounsfield units ............................................ 39

4.3 Calibration curve and blind tests .................................................... 41

4.4 Measurements and absorbed doses .............................................. 43

5. CONCLUSIONS ............................................................................. 45

6. ACKNOWLEDGMENTS ................................................................. 46

7. REFERENCES .................................................................................. 47
1. INTRODUCTION

The aim of radiation therapy is to deliver high doses to the target to achieve an increased local tumor control while protecting the surrounding healthy tissue. The dose needed for local control and the dose tolerated by healthy tissue gives a narrow therapeutic window. Studies have shown that changes of 5% in dose results in 10–20% changes in tumor control probability and changes in normal tissue complication probabilities of 20–30%, Brahme (1984) and Chetty et al (2007). Therefore, high accuracy\(^1\) in the dose delivered clinically is required and quality assurance of machines, delivery techniques and treatments employed in radiation therapy are hence of big importance.

Radiation therapy delivery techniques are becoming more advanced and complicated, e.g. IMRT, IGRT (Image guided radiation therapy) VMAT (Volumetric modulated arc therapy) and Tomotherapy and are adopted in a fast pace. The advances are driven mainly by technological development of the apparatus for radiation treatment and imaging, giving a significant risk of random and systematic errors that needs to be investigated in order to achieve high quality treatments.

The absorbed dose given in external radiation treatments is coupled to measurements for determination of absorbed dose to water under reference conditions using a calibrated ionization chamber traceable to a standard laboratory, Andreo et al (2000). In Sweden, it is required to calibrate all ionization chambers used clinically at the Swedish radiation safety authority SSM with two years interval, (SSM, 2008a and 2008b). All clinics should regularly participate in external dose verifications in reference conditions performed by an independent organization. The European organization ESTRO offers dose verification for external radiation therapy with high energy photons and electrons in reference conditions performed with TLD (thermoluminescence dosimetry), Dutreix et al (1994) and Ferreira et al (2000). The International Atomic Energy Agency, IAEA offers dose verification for clinical applications in reference conditions using TLD, Izewska (2002), Izewska (2007) and Mehta (1995). The National Physical Laboratory, NPL, provides a mailed reference dosimetry service for \(^{60}\)Co γ-rays and megavoltage photon beams using alanine, (www.npl.co.uk).

\(^1\) The accuracy of a measurement describes how well the result of the measurement agrees with the true value of the measurand.
When delivering a radiation treatment several factors, other than accelerator output in reference conditions, contribute to the uncertainties in the dose delivered to the tumor and healthy tissue. Therefore an effective audit system where influences from the whole treatment chain are taken into account would be of great value to evaluate the total combined uncertainty in the delivered dose.

In some countries e.g. USA, Belgium and Korea, dose audits for the whole treatment chain or parts of it are performed utilizing anthropomorphic phantoms and dosimetry systems like TLD, Youngyih et al (2008), Molieu et al (2005), Swinnen et al (2002), Bridier et al (1999), Allahverdi et al (1999) and Low et al (1997). In a study performed by RPC (Radiological Physics Center, MD Anderson Cancer Center) in USA, 20% of dose audit measurements did not pass the verification criteria of less than 7% dose difference or 4mm distance to agreement. Furthermore, less than 70% of the clinics involved in the study passed the criteria at the first verification, Ibbott (2008). During summer 2010, dose audits are performed for all radiation therapy clinics in Sweden by Tommy Knöös and Joakim Medin as a project for the Swedish Radiation Protection Authority. However, these measurements are performed only once. There are no such audit systems available on a regular basis in Sweden today.

Ionization chambers, TLDs, Si-diodes and film dosimetry among others have been the most utilized dosimetry systems for radiation therapy applications over the years. EPR dosimetry is a dosimetry system available today with the potential to become a complement to TLD. TL dosimetry with lithium fluoride has been the material used in clinical applications for many years with its advantages of high sensitivity, dosimeter reusability, low energy dependence and a 2% reproducibility (1 SD) in dosimeter reading in the radiation therapy dose range, Essers and Mijnheer (1999), Mobit et al (1996) and Kron (1995). Vestad et al (2004b) made an objective comparison of dosimeter reading and energy dependence between EPR dosimetry with lithium formate and TL dosimetry with lithium fluoride rods. TLDs have a higher sensitivity at low doses. However, the dose response for lithium flouride is supralinear for doses above 1 Gy. Lithium formate has a linear dose response with a high precision\(^2\) for doses above 2 Gy and with lower energy dependence in comparison with lithium fluoride. TLDs have a readout process that erases the signal which makes the dosimeters reusable. For EPR dosimetry in contrast to TL dosimetry, the readout process is non destructive to the signal which facilitates for several readouts.

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\(^2\) The precision of a measurement describes the reproducibility of repeated measurements.
Even EPR dosimetry with alanine has been proven to be advantageous in different applications. Mehta and Girzikowsky et al (1996) presented a study that evaluated alanine-EPR dosimetry system as an alternative to TLDs and EPR dosimetry became a standard technique at the IAEA for measurements of high doses for industrial applications. Alanine is close to water equivalent with low energy dependence regarding megavoltage photon energies, Bergstrand et al (2003), but has low sensitivity at low doses which is a drawback for its usefulness in medical radiation treatment dosimetry applications, Nagy et al (2002). The NIST (National Institute of Standards and Technology) provides certified irradiations of dosimeters with $^{60}$Co gamma rays for high-dose applications with alanine, (www.physics.nist.gov). The NPL audit service with alanine dosimeters provides dose determinations in the 5-10 Gy dose range with an uncertainty of ±1% (1 SD). However, the size of the alanine dosimeters NPL uses is about 20 times larger than the lithium formate dosimeters used in the present work. With increased dosimeter size and doses, the accuracy of the EPR dosimetry system increases.

In a study with the aim to find a more sensitive dosimeter material than alanine, new materials for EPR dosimetry were investigated and formates and dithionates were found to be more sensitive than alanine, Lund et al (2001). In another program to develop an EPR dosimeter suited for clinical use, different polycrystalline samples were examined and lithium formate monohydrate was the best candidate, with a linear dose response in the dose range from 0.2 to 1000 Gy, (Vestad et al 2003). Gustafsson et al (2008) showed that the lithium formate EPR dosimeter response was independent of the dose rate and the beam quality in the ranges used for IMRT treatments. Antonovic et al (2009) showed that the EPR system with lithium formate is suitable (as an alternative to LiF TLD) for high dose rate brachytherapy applications, and Waldeland et al (2010) showed its feasibility for accurate dose verification of stereotactic radiosurgery (SRS). A standardized EPR dosimetry system with lithium formate has been developed and characterized at the University Hospital in Linköping.

The aim of the present work is to design and evaluate a mailed dosimetry audit system for external dose verification where influences from the whole treatment chain (from CT scanning, to contouring of structures, treatment planning and treatment delivery) are taken into account, using EPR dosimetry with lithium formate.
1.1 Strategy

The EPR dosimetry system with lithium formate is suitable for mailed dose verification applications due to the robustness of the dosimeters. The EPR dosimeters with lithium formate have a wide measurement dose range (which facilitates measurements in both OARs and target), low energy dependence, low signal fading and a non destructive signal readout that provides several readouts to improve the statistics (further discussed in section 2.2). The readout of the dosimeters is performed with an EPR spectrometer (further discussed in section 3.3) with time and expense requirements comparable to TL dosimetry, Vestad *et al* (2004 b). Also, for accurate measurements the readout of the TLDs requires a very strict time schedule. This would be difficult to achieve in a mailed audit system, resulting in a decreased accuracy. The EPR signal stability over time of lithium formate makes such dosimeters more appropriate for mailed dose verifications and is the dosimetry system used in the present work. Hitherto, Linköping’s University is the only site in Sweden using EPR for dosimetry.

The strategy for the present work was to perform measurements on close to clinical cases and evaluate the dose in relevant points with influences from the whole treatment chain taken into account, using an audit phantom designed to be relevant for the head-and-neck region with target and OARs (further discussed in section 3.1) The doses determined using the EPR dosimeters were compared to the planned doses (further discussed in section 4).

The audit phantom was CT scanned both with a Siemens CT and a GE CT. Both CT studies were imported into the Helios/Eclipse (Varian) treatment planning system. Since the quality of the CT study could affect the quality of the treatment plan, two histograms over a ROI (region of interest) were generated for comparison of HU and the possible influence on the dose distribution (further discussed in section 4). The target and OARs were contoured and an IMRT treatment plan was created. The volumes of the phantom structures were measured on the phantom and compared to the values estimated by the TPS for both CT studies (further discussed in section 3.6.1). Since the Siemens scanner is the one normally used for treatment planning at the University Hospital in Linköping, the Siemens study was chosen as basis for the plan used for comparison with the determined doses. Two calculation algorithms were compared; Pencil Beam and AAA (analytical anisotropic algorithm), where AAA is the more accurate algorithm. Hence, the plan used for comparison with the determined doses was calculated with AAA.
In order to check the quality of the IMRT treatment plan compared to other clinical plans, a verification measurement was performed according to the plan verification method normally used in the clinic (further discussed in section 3.5.2). Also treatment table attenuation measurements and accelerator output measurements were performed (further discussed in section 3.5.2). The accelerator output and attenuation in the treatment table were corrected for in the determination of the planned doses.

In order to test the precision and accuracy of the dosimetry method three blind tests containing three dosimeters each, were prepared for irradiations to three different doses unknown to the person responsible for EPR dosimeter readout, (further discussed in section 3.6.2). These blind tests became extra important for the evaluation of the method since the limitation of time for the project made repetition of the audit measurement out of the time frame. Also, in order to test the performance of the of the treatment planning system, a plan on a virtual phantom with the same shape and dimensions as the calibration phantom was created to deliver the same doses as given during the blind test. The results were compared with the results from the ionization chamber.

The IMRT treatment was delivered to the audit phantom using DMLC (Dynamic Multi Leaf Collimator) technique. The absorbed dose to water in the target and OARs was determined using the signal from the EPR dosimeters and were compared to the results provided by the treatment planning system (further discussed in section 3.6.2).
1.2 IMRT versus Conformal Radiation Therapy

Conformal radiation therapy, CRT, is delivered by matching the shape of the beam to the target projection using computers and CT systems. This yields a dose distribution that encloses the tumor and avoids healthy surrounding tissue as much as possible. Using multi leaf Collimator, MLC, the beam is shaped so that exposure to normal tissue is minimized. The radiation beam has a uniform intensity but can be modified with filters or wedges.

Although the aim of the CRT is to target the tumor more precisely while protecting as much of the surrounding healthy tissue as possible, the incoming radiation fluence of the CRT is homogenous and cannot encompass the tumor exclusively. This is why the need of modulating the fluence within the field rose, Brahme et al (1982), and the Intensity Modulated Radiation Therapy, IMRT, was developed (see figure 1).

Figure 1: A comparison between a) Conventional radiation therapy, b) Conformal radiation therapy and c) Intensity modulated radiation therapy. Conventional radiation treatments were delivered with fields of a rectangular shape that could be altered with blocks and wedges. The MLC provided convenient conformation of the conformal radiation therapy fields. IMRT deliver the treatment via fluence modulation.

IMRT is a development of the conformal radiation therapy and is a combination of several intensity-modulated beams. Every field is divided into several minor fields with different fluencies within the same treatment field, which provides a highly conformal dose distribution, especially when the tumor volume has a concave surface. The treatment consists of a combination of intensity-modulated fields coming from different beam directions, (see figure 2).
**Figure 2:** A transversal slice of the phantom used in the present work with the planning target volume, PTV (target) and the organs at risk, OARs (OAR1= lung, OAR2= salivary glands and medulla). This is a simple sketch of three beams each with a modulated fluence to achieve the desired dose to the PTV while sparing the OARs. Typically, rays that go through critical structures have a reduced beam intensity while rays going primarily through the target volume, have an increased beam intensity. This is only a simple illustration to understand the principles in IMRT and it is not a suggestion for treatment.

Various methods for the delivery of intensity-modulated fields exists and several approaches to IMRT have been developed but MLC based IMRT techniques, are today most used and can be delivered by two methods:

- *Static* IMRT, segmented MLC mode, referred to as SMLC
- *Dynamic* IMRT, dynamic MLC mode, referred to as DMLC

DMLC, which is the delivery technique used at the university hospital in Linköping, is based on continuous irradiation while the MLC-leafs move with varying speeds, according to a predetermined trajectory giving the desired dose distribution. The treatment time is minimized compared to the SMLC technique.

To generate the desired beam shapes and dose distribution, the individual treatment pattern of the IMRT is carefully planned using *inverse treatment planning*, ITP, algorithms. In ITP, the computer adjusts the beam shapes and intensities to best meet the desired dose distribution.
IMRT is the preferable treatment technique, compared to CRT, for complicated cases e.g. tumors in the head-and-neck region which is very complex with air cavities, soft tissues and bony structures allocated in a very complex way. Kam et al (2003) showed that IMRT improved the tumor coverage while sparing the healthy tissue and offered a room for dose escalation. However, with advanced techniques the risk for significant uncertainties in the delivered dose is increased and needs to be investigated.
2. THEORY

2.1 Basic EPR theory

EPR spectroscopy is based on the principles of quantum mechanics and that a molecule or an atom has discrete states, each with a corresponding energy. EPR spectroscopy is used for measuring the energy differences $\Delta E$ between the different states to analyze the composition and structure of materials with paramagnetic compounds, and can also be used to quantify the amount of radicals in the material.

EPR dosimetry measures the amount of molecules with unpaired electrons, radicals, produced in a material when irradiated and is based on EPR spectroscopy. The radicals produced in the material are very reactive. However, in lithium formate, the free radicals are trapped in the crystalline structure and are therefore long-lived (further discussed in section 2.2).

Because all electrons have a spin, and thereby a magnetic moment, $\mu$, they align either parallel or anti-parallel to an applied external magnetic field $B_0$. This is called the Zeeman effect. The electron is a spin $\frac{1}{2}$ particle and results in two possible energy states, $M_s = + \frac{1}{2}$ (spin up) which is the anti-parallel state and is of a higher energy and $M_s = - \frac{1}{2}$ (spin down) which is the parallel state and is of a lower energy. The energy of a state, $E$, varies with the magnitude of $B_0$ according to:

$$E = M_s g_e \beta_e B_0$$ (1)

and therefore the energy difference, $\Delta E$, between the spin up and spin down energy states varies with $B_0$ according to:

$$\Delta E = g_e \beta_e B_0$$ (2)

where $g_e$ is the spin g factor for the free electron and is a proportionality constant that varies depending on the electronic arrangement of the radical and $\beta_e$ is the Bohr magneton.

In the absence of the external magnetic field, $B_0$, the two spin states have the same energy. But when exposed to $B_0$ the energies of the spin states diverge and the separation of energy states increases linearly with the increased $B_0$ (see figure 3). Hence, without an external magnetic field, there is no energy difference to measure.
Figure 3: The variation of the state energies with the increased magnetic field $B_0$ until absorption occurs as a peak.

The amount of unpaired electrons can be determined by exposing the material in the magnetic field $B_0$ to microwaves. When the frequencies are matching the resonance conditions, the microwaves will be absorbed according to Planck’s law:

$$\Delta E = h \nu$$

where $h$ is Planck’s constant and $\nu$ is the frequency of the microwaves.

To obtain a spectrum, the microwave frequency is normally kept constant while the magnetic field is scanned. The magnetic field $B_0$ is increased until the energy difference of the two spin states matches the energy of the microwave radiation giving a peak in the absorption (see figure 3).

In addition to the external magnetic field $B_0$, the unpaired electron experience a local magnetic field produced by nuclei in neighboring atoms that opposes or adds to $B_0$ depending on the alignment of the moment of the nucleus. These interactions are called hyperfine interactions. The hyperfine interactions causes splitting in the EPR signal and the absorption peak will be a superposition of components both higher and lower than $B_0$ causing a spectrum that could have several peaks, and also a broadening of the absorption peaks. Lithium formate gives a spectrum with only one peak, which is relatively narrow.

By modulating $B_0$ with a magnetic field, $B_m$, the resulting signal amplitude, $i$, will oscillate with the same frequency as the modulation frequency. Noise is then decreased by setting the detector to only record signals with the same frequency as the modulation frequency. The
amplitude of the detected signals will closely approximate the first derivative of the absorption curve, (see figure 4). Therefore, it is the peak-to-peak amplitude of the first derivative of the absorption curve that is taken as the signal amplitude which is used to determine the absorbed dose for the EPR measurements.

**Figure 4:** The absorption signal (upper graph) is modulated with a magnetic field $B_m$, giving the first derivative of the absorption signal (lower graph).
2.2 Lithium Formate EPR dosimetric properties

The EPR dosimetric properties of polycrystalline lithium formate monohydrate (HCO$_2$ Li H$_2$O, referred to as lithium formate in the present work) have been investigated due to the low sensitivity of alanine to be applied in dosimetry for clinical practice, A Lund et al (2001) and Vestad et al (2004 a). Two different radical species are produced when irradiating lithium formate with a dominating radical $'\text{CO}_2\text{'}$ trapped in the crystal matrix, Vestad et al (2004 a). EPR dosimeter readout is non-destructive to the signal which makes it possible to do several readouts to improve the statistics. Even integrated measurements between fractions are feasible. The reusability of the dosimeters is limited due to the accumulating signal. Nevertheless, this facilitates the opportunity to archive the dosimeters and re-analyze them when needed. Lithium formate has two to six times higher sensitivity than alanine (depending on read out procedure) and it exhibits no zero-dose signal. The dose response is linear in the dose range from 0.2 to 1000 Gy, Vestad et al (2003). Stability of the radicals produced when lithium formate is irradiated before readout (signal fading) was also investigated and it was shown that no significant signal fading during 28/ days was found, Gustafsson et al (2008). However, in an ongoing study performed at Linköping University, it was shown that there is a 5% signal fading during the first five days, (personal communication Sara Olsson). Nevertheless, the calibration and blind test measurements were performed during the same day as the audit measurement and hence the results became insensitive to fading. Before the system is used for a mailed dose audit, the signal fading will be further investigated in order to correct for it correctly. The EPR dosimetry system with lithium formate has been tested for clinical applications, Gustafsson et al (2008), Antonovic et al (2009) and Waldeland et al (2010). At Linköping’s University, a standardized method has been developed and tested.

No investigations of any possible dependence of temperature and humidity for lithium formate have been performed. Nagy et al (1999), performed systematic measurements of temperature dependence for alanine and it was shown that a signal dependence of the read out temperature was between 0.135-0.190% for doses between 20-100 kGy. It is likely to think that lithium formate has a temperature dependency of the same order of magnitude as alanine. Although, there is a concern for how the dosimeters could be affected by temperature during the transport between the clinics for the mailed dose audit. Higher temperature could result in higher thermal motion and hence faster fading. The lithium formate temperature dependency should be investigated for the mailed audit system.
Tissue equivalent materials are preferable as dosimeter materials for use in clinical dose verifications in radiation therapy. The atomic number and the density of the dosimeter are important aspects regarding attenuation and scattering of ionizing radiation. Lithium formate with an atomic number of 7.3 (water 7.5) and density of 1.26 g/cm$^3$ (water 1 g/cm$^3$) is closer to water in terms of absorption properties than alanine, with an atomic number of 6.8 and density of 1.45 g/cm$^3$, Vestad et al (2004). The dosimeters used in this study contain 10% paraffin and 90% lithium formate (further discussed in section 3.2) and have a density of 1.32 g/cm$^3$.

Since the size of the lithium formate dosimeters (4.5-5 mm) used in the present work (further discussed in section 3.2) is in the same order of magnitude as the size of the electron range in PMMA for a 6 MV photon beam (1-15 mm), the dosimeters are considered as medium size. Also, transient charged particle equilibrium (TPCE) is assumed throughout the dosimeter volume. Therefore, the dosimeters are regarded to act as a Burlin cavity. The ratio of mass energy absorption coefficients and the ratio of mass collision stopping power for lithium formate and alanine relative to water, plotted as a function of energy, shows the low energy dependence of lithium formate (see figure 5a and b). As seen in figures 5a and b, the ratios vary less with energy for lithium formate in comparison with alanine. The energy dependence of the dosimeter mixture used in this study is also shown in figures 5a and b.

![Mass energy absorption coefficient](image-url)

**Mass energy absorption coefficient**

- Lithium Formate
- 90% Lithium Formate + 10% Paraffin
- Alanine

a)
Figure 5: a) Mass energy absorption coefficients ratio of pure lithium formate, lithium formate dosimeter material and alanine relative to water, b) Mass collision stopping power ratio of pure lithium formate, lithium formate dosimeter material and alanine relative to water. The values for both mass energy absorption coefficients and mass collision stopping power values are acquired from the NIST, (www.physics.nist.gov). The collection of data in NIST is an extension and replacement of the calculations and values given in Seltzer 1993 and Hubbell (1982).

Gustafsson et al (2008) showed that the lithium formate EPR dosimeter response was independent of the dose rate and the beam quality in the ranges of relevance for IMRT treatments. In a master thesis project, “Investigation of energy and dose rate dependence in lithium formate EPR dosimeter”, Emelie Adolfsson (2009) showed that lithium formate has a decrease in dose response at low photon energies of relevance to brachytherapy (< 1 MeV). In the same study an indication of dose rate dependence was observed. However, after repeating the experiment a conclusion that eliminates dose rate dependency was drawn (Emelie Adolfsson personal communication).
3. MATERIALS AND METHODS

3.1 Phantom design

An anthropomorphic phantom was designed and constructed for an audit-system for external dose verification with influences from the whole treatment chain (from CT scanning, to contouring of structures, treatment planning and treatment delivery) taken into account, based on EPR dosimetry with lithium formate.

The idea behind the design was derived from an IMRT phantom designed for a remote monitoring program (Han Y et al 2008) and the phantom was manufactured at Linköping University Hospital.

Since IMRT, which is the treatment technique used in the present work, is often used to treat head and neck cancer, the inside of the phantom was designed to mimic the head-and-neck region with the tumor (target) encompassing the medulla (OAR). Other OARs are the salivary glands that are adjacent to the tumor, (see figure 6 b). Tissue substitutes are chosen so that their radiation interaction properties (energy attenuation and scattering properties) match those of the body tissue. PMMA (polymethyl methacrylate), with a density of 1.18 g/cm$^3$, was the choice of material for this phantom since it is near tissue equivalent and is readily available. A structure made of Teflon (density: 2.20 g/cm$^3$) resembling the spinal bones and an inhomogeneity in the form of an air cavity, were also included. The air cavity can be filled with a plug of foam plastic with density 0.14 g/cm$^3$ to mimic lung tissue. It should be mentioned that the air cavity was intended to mimic a lung. However, the material was delayed and the measurements were done with an air cavity instead of a lung.

The body of the phantom, the poles, the braces, the target, the salivary glands and the medulla were made of PMMA. At the center of every structure, a hole was drilled, three holes in the target. Seven cylindrical tubes also made of PMMA with an inner diameter of 5mm were inserted into the holes for dosimeter placement, (se figure 6 b). The structures go through the four cylindrical slices in the middle (see figure 6 c).
Economical and practical manufacturing concerns played an important role in the phantom design and led to the choice of a solid material to facilitate precise production. Due to manufacturing reasons, the cylindrical phantom consists of eight cylindrical slices tacked together with three cylindrical rods throughout the phantom, (see figure 6 a). The diameter of the phantom was 20 cm. The thickness of the cylindrical slices is 3 cm each, giving a total length of 24 cm when put together. The first and the last slices rest on braces, (see figure 6 c).
In order to eliminate the dependency on the person contouring the organs, the fit of the structures was accommodated in order to be well discriminated from the surrounding material, (see figure 10a) in section 3.5.1.

3.2 Manufacturing of dosimeter batch

The dosimeters were made manually following a method developed by Håkan Gustafsson (Gustafsson et al (2008)). The EPR dosimeters were made in the form of cylindrical pellets of polycrystalline lithium formate monohydrate (98%) (HCO$_2$ Li H$_2$O) obtained from Sigma-Aldrich and solid household paraffin ($C_n$H$_{2n+2}$, $n = 20 - 40$). The dosimeters consist of 90% lithium formate which is the active material and 10% paraffin which is used as a binder to make the dosimeters stable and non-fragile. One batch typically consists of 20-30 dosimeters.

The lithium formate was at first crushed in a mortar, then sieved in a strainer (Endecotts MINOR) to grain sizes between 180 and 300 µm. The powder was weighed to determine the amount of paraffin to be added. The paraffin and the powder were mixed and put in a beaker that was heated up to 90˚ C in an oven until the paraffin had melted. The paraffin’s melting point is between 54˚-56˚ C and the melting point for lithium formate is 94˚ C so the binder melts before the lithium formate crystals are damaged. The content of the beaker with the liquefied paraffin was thoroughly mixed before reheating. This procedure was repeated three times before a profound final mixing was performed, in order to produce a homogeneous powder of lithium formate and paraffin. The mixture was held in room temperature for an hour before manufacturing the batch, until the paraffin had solidified completely.

A manual tablet press was utilized for making the dosimeters, using 100 mg mixed powder. The cylindrical dosimeters of 5 mm height, (see figure 7), were weighed after being pressed and a maximum deviation in mass of ± 2 mg was tolerated, otherwise the dosimeter was excluded from the batch. For this study a batch of 29 dosimeters was manufactured. All dosimeters were stored under the same environment conditions to ensure signal homogeneity.

![Figure 7: A typical group of five dosimeters labeled for identification.](image-url)
Ten dosimeters were used for calibration curve determination (further discussed in section 3.5.3) and seven dosimeters were used for dose measurements. Three groups consisting of three dosimeters each were arranged for blind test measurements with three remaining dosimeters.

### 3.3 EPR measurements and readout

A BRUKER EleXsys E 580 spectrometer at Linköping University was utilized for all EPR measurements. The spectrometer was equipped with a standard cavity ER 4102ST. A WILMAD EPR quartz glass sample tube (Q-5M-6M-O-200 m-FB) with an inner diameter of 5 mm and flat bottom was employed for dosimeter placement in the cavity. The readout process of a whole batch including calibration dosimeters was performed in a single day due to spectrometer response variation from day to day. It is recommended that the readout process during the mailed audit measurement will be performed during a single day. However, should the readout process be divided into several days, a stable reference sample, e.g. manganese, should be fixed in the resonance cavity in order to supervise the spectrometer response variation from day to day and correct the signal for the spectrometer sensitivity. Nevertheless, this would result in a minor decrease of the accuracy. It is the peak-to-peak amplitude of the first derivative of the absorption spectrum, $P$ [dimensionless], divided by the mass of the dosimeters, $m$ [mg], that is measured as the signal amplitude, $l_w$ [mg$^{-1}$].

To ensure identical and reproducible positioning of the dosimeters in the cavity, the sample tube containing the dosimeter was placed on the notch of an in-cavity pedestal. Gustafsson et al (2008) optimized and standardized the settings of the spectrometer for lithium formate. For the present work, measurements were performed using a microwave power of 20 mW, a sweep width of 3 mT centered at 346 mT and with a time constant of 327.68 ms and a sweep time of 167.77 s. The modulation amplitude was set to 1.2 mT.

To increase the accuracy, five measurements of the same dosimeter were performed. Due to possible small variations in spectrometer sensitivity during a measurement session, the five measurements of each dosimeter were spread out over the day to avoid systematic errors in the spectrometer reading caused by time. The EPR signal was not smoothed filtered or manipulated in any way and was determined as the mean of all five readings.
3.4 Dosimeter batch quality control

It is important to check that all dosimeters respond equally to radiation before use. The spread of the dose response can be determined in terms of the relative standard deviation of the mean signal of the batch and should be less than 1 %. Tablets not fulfilling that condition are excluded from the batch.

All dosimeters of the batch were irradiated, ten at a time, to a dose $D_0$ using a PMMA phantom with dimensions of $6 \times 20 \times 20 \text{ cm}^3$ with an extra slab of 4 cm PMMA positioned on the phantom. Two inserts made of PMMA, that fit five dosimeters each, can be positioned in the middle of the phantom, (see figure 8). For a sufficient precision in dosimeter reading, the dose given to the dosimeters should be higher than 2.5 Gy due to the precision in the spectrometer, Vestad et al (2004 b), (see section 3.5.2).

![Figure 8](image)

**Figure 8**: a) The PMMA phantom used for the quality control and pre-irradiations, b) and c) the PMMA inserts that can be positioned in the middle of the phantom containing five dosimeters each.

The dosimeters were irradiated at 7 cm depth in PMMA in a field of area $10 \times 10 \text{ cm}^2$ and SSD (Source to Surface Distance) of 100 cm in a 6 MV photon beam using a Varian Clinac 600 C/D linear accelerator at Linköping University Hospital.
To ensure the same dose to each dosimeter independently of position and inhomogeneities within the radiation field, the dosimeters were rotated in the phantom, both with each other in the inserts and also by letting the two inserts change place with each other (see figure 9). Ten rotations were made with an irradiation divided into ten fractions, giving the dosimeters a total dose of $D_0 = 3$ Gy.

**Figure 9:** An illustration of the rotation scheme of the inserts with each other and the rotation of the dosimeters with each other.

Since the EPR dosimeter readout is non-destructive, the signal corresponding to $D_0$ is considered to be the background signal, $b$, of the batch (see section 3.5.3).

### 3.5 Measurements

All irradiations described in the following were performed in a 6 MV photon beam using a Varian Clinac iX linear accelerator at Linköping University Hospital.

#### 3.5.1 CT scanning, contouring and treatment planning

The phantom was CT scanned twice using a Siemens SOMATOM Sensation Open and a GE Light Speed Ultra for comparison of Hounsfield units and dose distribution. During the scan the dosimeters were replaced with PMMA inserts to avoid measuring the dose from the CT scan. The slice thickness was 1 mm when scanning with the Siemens CT and 2.5 mm when
scanning with the GE CT. The structures were well differentiable from the immediate surroundings in both CT studies (see figure 10a and b). The Helios/Eclipse (Varian) treatment planning system, TPS, was used to contour the phantom structures (see figure 10c), and to optimize and calculate the IMRT treatment plan. The treatment plan consisted of seven coplanar beams separated by 51°-52°, (see figure 11).

**Figure 10:** a) A transversal Siemens CT slice of the phantom with the target and OARs well differentiated from the surroundings, b) a transversal GE CT slice of the phantom with the target and OARs well differentiated from the surroundings, c) a transversal slice of the phantom with contoured body, OARs and target.
Figure 11: The dose distribution optimized and calculated by the TPS for the IMRT treatment of the target in the head-and-neck phantom.

3.5.2 Calibration and blind tests

Since lithium formate has linear dose response in the dose range from 0.2 to 1000 Gy, Vestad et al (2003), only two calibration points are needed to establish the calibration curve, Nagy (2000) and Gustafsson et al (2008). Hence the ten calibration dosimeters were divided into two groups five by five, corresponding to the two points needed to fit the curve (see figure 19). One of these groups was irradiated simultaneously with the ionization chamber (figure 12). The other five tablets were not given an additional dose. Their average signal, $b$, which was obtained from the homogeneity test that all dosimeters underwent represents the background signal of the batch and determined the lower point of the calibration curve (see figure 19).

An NE 2571 ionization chamber with a calibration coefficient traceable to the Swedish Secondary Standards Dosimetry Laboratory was used for the calibration and blind test measurements. The absorbed doses to a small volume of water in PMMA were determined
using the $N_{D,w}$ coefficient of the ionization chamber and the beam quality correction factor $k_{Q,Q0}$ valid for the 6 MV photon beam under reference conditions; 10 x10 cm$^2$ field and SSD of 100 cm in a water phantom at 10 cm depth. The measurements were performed using a PMMA phantom with dimensions of 20 x 20 x 20 cm$^3$. In other respects care was taken to match the reference conditions as closely as possible in order to reduce the uncertainties in $k_{Q,Q0}$ introduced by using a PMMA phantom instead of water. Recommendations and a discussion on how to do this, is given by Seuntjens et al (2005). Two inserts made of PMMA, one that fit five dosimeters and one that fit the ionization chamber, were used and positioned at a depth of 5 cm in the middle of the phantom, (see figure 12). To reach a depth where the beam is as homogeneous as possible and corresponds to almost 10 cm in water, an extra slab of 3 cm PMMA was positioned on the phantom. At 8 cm depth in PMMA the beam homogeneity is within 0.5% in a field of area 10 x 10 cm$^2$ and SSD (Source to Skin Distance) of 100 cm. This was previously measured for the accelerator used for the measurements of the present work.

![Figure 12: An illustration of the calibration set-up viewed from above. Not to scale.](image)

Both calibration tablets and blind test dosimeters were irradiated together with the ionization chamber.

To ensure the same dose to each dosimeter independently of position and inhomogeneities within the radiation field, the calibration dosimeters were rotated in the phantom (see figure 13). Five rotations were made with an irradiation divided into five fractions, giving the dosimeters a total dose of $D_e = 11.22$ Gy.
In order to test the precision and accuracy of the current dosimetric method, three groups containing three dosimeters each, were irradiated simultaneously with an ionization chamber to doses in the interval 1 - 9 Gy, unknown to the person responsible for EPR dosimeter readout.

The values of the determined absorbed doses in water from the blind tests with the estimated relative standard deviation were compared to the determined absorbed dose in water values from the ionization chamber.

In order to test the performance of the TPS in a simple and homogenous set up, a plan for the calibration and blind test irradiations was created on a virtual PMMA phantom with the same shape and dimensions as the actual calibration phantom. The planned doses were observed at the points where the dosimeters and the ionization chamber were placed. The results obtained from the TPS were compared to the results from the ionization chamber and the EPR dosimeters.
3.5.3 Pre treatment verification

In order to check the quality of the IMRT plan in comparison to the clinical plans used at Linköping University Hospital, a standard pre-treatment verification measurement was performed. The fields from the IMRT treatment plan were applied on a cylindrical polystyrene phantom shown in figure 14 a) resulting in a verification plan. Two RK 8305 ionization chambers, each with a calibration coefficient traceable to the Swedish Secondary Standards Dosimetry Laboratory, were used to determine the absorbed dose to water in two points. The chambers were positioned in relatively low dose-gradient regions within the target volume (see figure 14 b). An EPID (Electronic Portal Imaging Device), in the present work a Varian Portal Vision, was used to determine the 2D fluence for every field in the IMRT treatment plan. The determined point doses and fluence distributions were compared to the verification plan. The deviation between the determined and calculated dose distributions should be less than 3% in dose or have a distance to agreement, DTA, less than 3mm, P C Williams (2003). These criteria of dose difference and DTA are combined in an index called $\gamma$. The value of $\gamma$ in a point is $\leq 1$ when the criteria are fulfilled.

![Image](image-url)

**Figure 14:** a) the IMRT phantom used for IMRT verification measurements, b) the dose distribution from the original IMRT treatment plan substituted to the IMRT phantom with ionization chambers positions marked with $jk1$ for ionization chamber number one and $jk2$ for ionization chamber number two.
3.5.4 Audit measurement

The cylindrical audit phantom with inserts for EPR dosimeters was irradiated (see figure 15) according to the IMRT treatment plan giving the target a dose of 5 Gy.

Figure 15: The audit phantom positioned for IMRT treatment.

In order to avoid that the fluence at the location of one dosimeter is perturbed by the surrounding dosimeters, the dosimeters were placed into the structures according to figure 16.

Figure 16: Placement of the dosimeters in the phantom in order to avoid that the fluence at the location of one dosimeter is perturbed by the surrounding dosimeters. Not to scale.
The phantom was placed on a treatment table that is broader than the table normally used for patient treatments in the head-and-neck region. Therefore, two of the fields in the IMRT treatment plan pass through the treatment table. To correct for this, an attenuation measurement was performed for two gantry angels, 180° and 154° and or 206° (which are the angles on which the fields passes through the treatment table). And since IMRT plans consists of fields divided into small segments each with a modified fluence, the attenuation measurement was performed for not only a 10 x 10 cm$^2$ field size but also for a 3 x 3 cm$^2$ field size. In conformity with regular practice the output of the accelerator was checked immediately after delivering the IMRT treatment to the phantom.

Dose calculation algorithms have an important function in the TPS. Several algorithms are available today: Pencil beam, Collapsed Cone, and AAA among others and AAA is the most accurate algorithm available for the Eclipse (Varian) TPS, Gagné (2006). The absorbed dose to water values acquired from the TPS, were calculated with the AAA algorithm. The values of the determined absorbed dose to water in the different structures of the phantom $D_{w,EPR}$ with the estimated relative standard uncertainty were compared to the absorbed dose to water values provided by the TPS, $D_{w,TPS}$. 
3.6 Data analyses and uncertainties

3.6.1 Organ volumes and Hounsfield units

The volumes of the organs in the phantom were measured and compared to the volumes calculated by the TPS for both Siemens and GE CT images (see table 3).

The distribution of Hounsfield units in the two CT studies was compared. For this purpose, a ROI (region of interest) in the middle of a phantom slice was chosen according to figure 17 for each study and the HU:s in each ROI was compiled in a histogram (see figure 18a and b).

Figure 17: The ROI put in the middle of a phantom slice.
3.6.2 Absorbed dose to water determination

At the calibration and the blind test experiment the absorbed dose to a small volume of water, $D_{w,Q}$, at the depth of the ionization chamber, 8 cm in PMMA, was determined using the approach in TRS 398, Andreo et al (2000):

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}$$

where $M_Q$ is the reading of the ionization chamber corrected for recombination, $k_s$ (acquired with the two-voltage method) and pressure and temperature, $N_{D,w,Q_0}$ is the calibration coefficient in terms of absorbed dose to water traceable to the Swedish Secondary Standards Dosimetry Laboratory and $k_{Q,Q_0}$ is the beam quality correction factor valid for the 6 MV photon beam characterized by the tissue phantom ratio, $\text{TPR}_{20,10}$, under reference conditions. Since the lithium formate dosimeters were positioned at the same depth as the ionization chamber, the absorbed dose to water at the depth of the lithium formate dosimeters was assumed to be equal to $D_{w,Q}$. The calibration beam quality in terms of $\text{TPR}_{20,10}$, the quality correction factor $k_{Q,Q_0}$ and the recombination correction factor $k_s$ are presented in table 1.

<table>
<thead>
<tr>
<th>$\text{TPR}_{20,10}$</th>
<th>$k_{Q,Q_0}$</th>
<th>$k_s$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibration measurement</td>
<td>0.664</td>
<td>0.994</td>
</tr>
</tbody>
</table>

Table 1: Factors for absorbed dose to water determination at reference conditions according to TRS 398, Andreo et al (2000), and used for determination of the calibration dose

Linear regression was used to generate the calibration curve given by:

$$l = a \cdot D + b$$

where $l$ (mg$^{-1}$) is the EPR signal corresponding to the dose $D$ (Gy) given, $a$ (mg$^{-1}$Gy$^{-1}$) is the slope of the curve and $b$ (mg$^{-1}$) is the non-zero intersection with the signal axis (y-axis).

Equation (5) was used to deduce the slope of the calibration curve according to:

$$a = \frac{l_c - b}{D_c} = \frac{l_{cc}}{D_c}$$

where $D_c$ is the dose given during the calibration, $l_c$ is the signal corresponding to $D_c$ and $l_{cc}$ is the calibration signal corrected for background.
No conversion from dose to water to dose to lithium formate is needed since the calibration was performed in terms of absorbed dose to water and the absorbed dose in the different structures of the phantom will be compared to the absorbed dose values calculated by the TPS which also are given as absorbed doses to water.

The absorbed dose to water to the blind tests and structures in the audit phantom, \( D_w \), is deduced from equation (5) using the calibration curve parameters \( a \) and \( b \) and the EPR signal from the dosimeter used, \( l_w \), according to:

\[
D_w = \frac{l_w - b}{a} = \frac{l_x}{a}
\]  

(7)

where \( l_w \) [mg\(^{-1}\)] is signal from the EPR dosimeter used and \( l_x \) is the background corrected signal.

### 3.6.3 Uncertainty analyses

The dose, \( D_w \), as mentioned earlier, is determined according to equation (7) by dividing the EPR signal, \( l_x \), by the slope of the calibration curve, \( a \). The EPR signal is corrected for the background signal, \( b \), which is the signal corresponding to the dose \( D_0 \) from the batch quality control. Hence, the relative uncertainty in dose is calculated by applying the uncertainty propagation law on equation (7) according to:

\[
\left( \frac{u(D_w)}{D} \right)^2 = \left( \frac{u(l_x)}{l_x} \right)^2 + \left( \frac{u(a)}{a} \right)^2
\]  

(8)

The first term in equation (8) concerns the uncertainty in the background corrected EPR signal. The EPR signal from a dosimeter, \( l_x \), is the peak-to-peak amplitude, \( P_x \), of the absorption spectrum, divided by the mass of the dosimeters, \( m_x \) [mg] and therefore:

\[
l_x = \left( \frac{P_x}{m} \right)_x = l_w - b = \left( \frac{P_x}{m} \right)_w - b
\]  

(9)

where \( \left( \frac{P_x}{m} \right)_w \) is the signal including the background signal.

The uncertainty in a single EPR dosimeter signal depends on the uncertainties in both the signal \( l_w \) and the background signal \( b \), calculated by applying the uncertainty propagation law on equation (9) according to:
\[ u^2(l_x) = u^2(l_w) + u^2(b) = u^2\left(\frac{P_m}{m_w}\right) + u^2(b) \]

\[ = \left(\frac{1}{m_w} \cdot u(P_w)\right)^2 + \left(\frac{P_w}{m_w^2} \cdot u(m_w)\right)^2 + u^2(b) \]

(10)

and the uncertainty in the background is given by:

\[ u(b) = \frac{1}{\sqrt{N}} \cdot u\left(\frac{P}{m}\right)_b \]

(11)

where \( u(P/m)_b \) is the standard uncertainty\(^3\) of the batch signals obtained from the quality control of the batch and \( N \) is the number of the dosimeters used, which in the present work is five.

The relative uncertainty in the dosimeter signal will be given by the following:

\[ \left(\frac{u(l_x)}{l_x}\right)^2 = \left(\frac{u(l_w)}{l_x}\right)^2 + \left(\frac{u(b)}{l_x}\right)^2 \]

(12)

where \( l_w \) [mg\(^{-1}\)] is signal from the EPR dosimeter used and \( l_x \) is the background corrected signal. The dosimeter signal also depends on spectrometer sensitivity variation, which is a type B uncertainty. This was previously measured and a standard uncertainty of 0.3% was compiled. However, efforts were made in order to reduce type B uncertainties, e.g. storing all dosimeters under the same environmental conditions, weighing of dosimeters before and after readout and spreading out the five readouts of a single dosimeter during the day. Therefore, type B uncertainties were regarded as negligible, Antonovic et al (2009).

The second term in equation (8) concerns the uncertainty in the slope of the calibration curve. The slope of the calibration curve, \( a \), is given by the signal of the dosimeters used in the calibration against the ionization chamber divided by the corresponding applied dose. Applying the uncertainty propagation law on equation (6), the uncertainty in \( a \) is given by:

\[ \left(\frac{u(a)}{a}\right)^2 = \left(\frac{u(l_{cc})}{l_{cc}}\right)^2 + \left(\frac{u(D_c)}{D_c}\right)^2 \]

(13)

\(^3\) It is the standard uncertainty of the mean that is referred to as the standard uncertainty in the present work.
where \( \left( \frac{u(l_{cc})}{l_{cc}} \right)^2 \) is background corrected calibration signal estimated according to equation (10) and \( \left( \frac{u(D_c)}{D_c} \right)^2 \) is the relative uncertainty in the calibration dose, assumed to be equal to the estimation for the absorbed dose to water in the users beam in TRS 398, Andreo et al (2000). However, in order to take into account the uncertainty for use of the ionization chamber in a PMMA phantom instead of water phantom, the uncertainty in the absorbed dose to water at the calibration was estimated to be somewhat higher 1.7% than the proposed value (1.5%) for the determination of absorbed dose to water in the users beam in TRS 398, Andreo et al (2000). The increased uncertainty in the calibration dose is mainly due to an increased uncertainty in the \( k_{Q,Q_0} \) factor. The calibration was performed using an NE 2571 ionization chamber, calibrated against a substandard (NE 2571 ionization chamber) with a calibration coefficient obtained at the Swedish Secondary Standards Dosimetry Laboratory. Any possible contribution to the total relative uncertainty of the covariance between \( a \) and \( b \) is negligible, Antonovic et al (2009).

An estimate of the relative uncertainty in dose is deduced according to equation (8). All the components contributing to the uncertainty in the slope of the calibration curve, \( a \), and consequently also to the uncertainty in the dose are listed in table 2.

<table>
<thead>
<tr>
<th>Component</th>
<th>Notation</th>
<th>Relative standard uncertainty (%)</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background signal</td>
<td>( u(b) )</td>
<td>0.4</td>
<td>A</td>
</tr>
<tr>
<td>Calibration signal</td>
<td>( u(l_{cc}) )</td>
<td>0.4</td>
<td>A</td>
</tr>
<tr>
<td>Calibration dose</td>
<td>( u(D_c) )</td>
<td>1.7</td>
<td>B</td>
</tr>
<tr>
<td>Calibration curve slope</td>
<td>( u(a) )</td>
<td>1.8</td>
<td>A</td>
</tr>
<tr>
<td>Target signal</td>
<td>( u(l_{target}) )</td>
<td>0.9</td>
<td>A</td>
</tr>
<tr>
<td>Target Dose to water</td>
<td>( u(D_{w,target}) )</td>
<td>1.9</td>
<td>A+B</td>
</tr>
</tbody>
</table>

Table 2: Components contributing to the uncertainty in the absorbed dose to water in e.g. target1.
4. RESULTS AND DISCUSSIONS

4.1 Dosimeter batch quality control

In the present work, the relative standard deviation of the mean signal of the batch, consisting of 29 dosimeters, was 0.87% and the batch was considered successful.

4.2 Organ volumes and Hounsfield units

The measured phantom volumes had no significant deviation in comparison with the volume values obtained from the TPS for both CT studies. They agreed within 2.5% for smaller structures (medulla and the salivary glands) and within 5% for larger structures (body, target and the air cavity). The difference between the TPS values from the Siemens study and GE’s CT study is due to the different slice thickness values used, (Siemens 1 mm and GE 2.5 mm).

<table>
<thead>
<tr>
<th>Organ</th>
<th>Measured (cm³)</th>
<th>$TPS_1$ (cm³)</th>
<th>$TPS_1 - Measured$ (cm³)</th>
<th>$\frac{TPS_1 - Measured}{Measured}$ (Relative difference)</th>
<th>$TPS_2$ (cm³)</th>
<th>$TPS_2 - Measured$ (cm³)</th>
<th>$\frac{TPS_2 - Measured}{Measured}$ (Relative difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body</td>
<td>7665.5</td>
<td>8054.5</td>
<td>389.0</td>
<td>5.1</td>
<td>7951.9</td>
<td>286.4</td>
<td>3.7</td>
</tr>
<tr>
<td>Air cavity</td>
<td>332.4</td>
<td>345.2</td>
<td>12.8</td>
<td>3.9</td>
<td>337.8</td>
<td>5.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Medulla</td>
<td>13.8</td>
<td>14.1</td>
<td>0.3</td>
<td>2.2</td>
<td>13.5</td>
<td>-0.3</td>
<td>-2.2</td>
</tr>
<tr>
<td>PTV</td>
<td>728.7</td>
<td>725.8</td>
<td>-2.9</td>
<td>-0.4</td>
<td>710.4</td>
<td>-18.3</td>
<td>-2.5</td>
</tr>
<tr>
<td>Parotis</td>
<td>150.3</td>
<td>152</td>
<td>1.7</td>
<td>1.2</td>
<td>148.5</td>
<td>-1.8</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Table 3: Measured organ volumes compared to the TPS calculated volumes from the Siemens CT study ($TPS_1$) and the GE CT study ($TPS_2$).

For comparison of the HUs distribution, two histograms compiled for both Siemens and GE CT studies are presented in figures 18a and b.

In the histograms, the peak around 1000 HU corresponds to the Teflon. PMMA is normally around 120 HU and air has -1000 in HU.
As seen in the HU histograms (figures 18a and b), the Siemens study contains more noise resulting in a larger spread of the HU (broader peaks) in comparison to the GE study. The noise depends on many factors such as dose, detector size and reconstruction filters. Nevertheless, the absorbed doses and the dose distribution were not affected by this spread. The absorbed doses were within 0.5% agreement in comparison between the Siemens and GE CT studies.
4.3 Calibration curve and blind tests

The calibration curve was fitted to the data points acquired from the calibration and is presented in figure 19. The uncertainty bars indicate the standard uncertainty (1 SD) in the data points.

Figure 19: The calibration curve. $D_c$ is the dose given to one of the groups giving an average signal from the five dosimeters $\bar{I}_c$ and $b$ is the background signal corresponding to $D_0$ of the other group which was not further irradiated.

The results from the blind tests, $D_{w,EPR}$, with uncertainties and the results from the ionization chamber, $D_{w,ion\.chamber}$, are presented in table 4 and figure 20. The doses obtained from the EPR dosimeters agreed with the results from the ionization chamber, the relative differences between EPR and ionization chamber measurements are within 1% and well below the calculated uncertainties in the EPR measurements.
Figure 20: Absorbed dose to water obtained from the EPR dosimeters plotted as a function of the absorbed dose to water obtained from the ionization chamber with uncertainties for the blind tests. The uncertainty bars indicate the standard deviation in the data points.

Table 4: Determined absorbed dose to water from the ionization chamber and EPR dosimeters of the blind tests.

<table>
<thead>
<tr>
<th></th>
<th>Blind test 1</th>
<th>Blind test 2</th>
<th>Blind test 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D_{w,ion.chamber}$ (Gy)</td>
<td>1.53</td>
<td>3.58</td>
<td>7.66</td>
</tr>
<tr>
<td>$D_{w,EPR}$ (Gy)</td>
<td>1.51 ± 0.03</td>
<td>3.54 ± 0.07</td>
<td>7.68 ± 0.16</td>
</tr>
<tr>
<td>$D_{w,EPR} - D_{w,ion.chamber}$ (mGy)</td>
<td>-18</td>
<td>-38</td>
<td>22.0</td>
</tr>
<tr>
<td>$\frac{D_{w,EPR} - D_{w,ion.chamber}}{D_{w,ion.chamber}} = Relative difference (%)$</td>
<td>-1.2</td>
<td>-1.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Calculated relative standard uncertainty (%)</td>
<td>2.0</td>
<td>2.0</td>
<td>2.1</td>
</tr>
</tbody>
</table>

The doses obtained from the virtual PMMA phantom measurement deviated from the doses acquired from the ionization chamber during the blind test measurement with -1.4%. This deviation can be explained with the variations in the accelerator output.
4.4 Measurements and absorbed doses

The pre-treatment verification measurement with ionization chambers showed an agreement between determined and calculated dose to be within 2% which is within the acceptance criteria for a clinical plan. The EPID measurements showed that \( \gamma > 1 \) in less than 1.5% of the field area for all fields in the plan. The measured treatment table attenuation was 3.3% and 2.7% for 3 x 3 cm\(^2\) fields for the 154˚ and 180˚ angles respectively and 2.1% and 1.8% for 10 x 10 cm\(^2\) fields for the 154˚ and 180˚ angles respectively. The attenuation was included in the determination of the planned dose by correcting the contribution to the dose from the two fields penetrating the treatment table for the attenuation for small fields at 154˚.

The absorbed doses in the target and OARs in the audit phantom with uncertainties determined with EPR and the planned doses acquired from the TPS are presented in table 5.

<table>
<thead>
<tr>
<th>Structure</th>
<th>( D_{w,EPR} ) (Gy)</th>
<th>Deviation (Gy)</th>
<th>( D_{w,TPS} ) (Gy)</th>
<th>( \frac{D_{w,EPR} - D_{w,TPS}}{D_{w,TPS}} ) = Relative difference (%)</th>
<th>Calculated relative standard uncertainty (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air cavity</td>
<td>1.74 (1.67)</td>
<td>± 0.07 (0.04)</td>
<td>1.59</td>
<td>147.1 (75.2)</td>
<td>8.90 (4.41)</td>
</tr>
<tr>
<td>Medulla</td>
<td>2.83</td>
<td>± 0.06</td>
<td>2.87</td>
<td>-39.6</td>
<td>-1.4</td>
</tr>
<tr>
<td>Target1</td>
<td>5.03</td>
<td>± 0.1</td>
<td>5.13</td>
<td>-88.6</td>
<td>-1.7</td>
</tr>
<tr>
<td>Target2</td>
<td>4.74</td>
<td>± 0.1</td>
<td>4.92</td>
<td>-182.3</td>
<td>-3.7</td>
</tr>
<tr>
<td>Target3</td>
<td>5.03</td>
<td>± 0.1</td>
<td>5.16</td>
<td>-125.3</td>
<td>-2.4</td>
</tr>
<tr>
<td>Parotis DX</td>
<td>1.21</td>
<td>± 0.02</td>
<td>1.19</td>
<td>27.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Parotis SIN</td>
<td>1.20</td>
<td>± 0.02</td>
<td>1.21</td>
<td>-16.0</td>
<td>-1.3</td>
</tr>
</tbody>
</table>

Table 5: Determined absorbed doses in water in the audit phantom structures, compared to planned doses.
The absorbed doses are within 4% agreement except for the absorbed dose in the air cavity. One of the readings of the dosimeter used in the air cavity deviated substantially from the mean giving the assumption of being an outlier\(^4\). Since no other explanation could be found, no elimination of the outlier was performed. However, the absorbed dose in the air cavity gets an agreement within 4.5% when eliminating the outlier value (the value presented in brackets in table 5) i.e. using only the signals from the four readings that do not have a considerable deviation from the mean.

In studies evaluating and quantifying the differences in dose distribution between the dose calculation algorithms, it was shown that there are evident differences between the algorithms and that collapsed cone convolution performed better than AAA when compared to Monte Carlo, Hasenbalg \textit{et al} (2007). Fogliata \textit{et al} (2007) showed that calculation algorithms are not adequate especially for small fields in low density media. Therefore, it is of interest to evaluate the absorbed dose in lung and the results acquired for the air cavity are hence considered satisfactory.

There are several general recommendations of uncertainty limits in delivered dose. According to Brahme the relative standard uncertainty of the mean dose in the target volume should be less than 3\% (1 SD) (Brahme 1988). Mijnheer \textit{et al} (1987) proposes a combined uncertainty (of random and systematic errors) in the absorbed dose delivery to be within 3.5\% (1 SD). ICRU 24 (1976) concluded an accuracy of \(\pm 5\%\) in the delivered absorbed dose to a target volume, (ICRU 1976). Since delivery techniques e.g. IMRT, are more advanced and complicated, it may be difficult to achieve less than 3\% total uncertainty in practice for more than one standard deviation. Hence, it is more common to refer to ICRU 24 (1976) value of \(\pm 5\%\) accuracy in the delivered dose. In an audit measurement performed in reference conditions using TL- dosimeters, RPC considered an agreement within 5\% satisfactory.

Withal, the absorbed doses from the audit phantom measurements, apart for the air cavity, have an agreement within the calculated uncertainty for two standard deviations.

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\(^4\) The readings in a spectrometer have a randomized distribution described by a Gaussian curve with some values in the tails of the Gaussian curve that deviate considerably from the mean, well outside 3 SD. These values are called outliers.
5. CONCLUSIONS

This work shows promising initial results for an audit system. This is just the beginning of a project for dose verifications with influences from the whole radiation therapy treatment chain taken into account.

The reconstructed and measured volumes of the audit phantom structures agreed within 2.5% for smaller structures and within 5% for larger structures. The comparison of HU in the CT studies showed a larger spread of the HU in the Siemens study compared to the GE CT study. However, the spread did not affect the absorbed doses and dose distributions. They had an agreement of 0.5% in comparison between the Siemens and GE CT studies.

For the blind tests, the doses obtained from the EPR dosimeters agreed with the results obtained from the ionization chamber within 1% and are well below the calculated uncertainties in the EPR measurements.

All the absorbed doses from the audit phantom measurements, apart for the air cavity, have a 4% agreement. This deviation is not covered by the calculated standard uncertainty. However, the deviation does fall within two standard deviations, corresponding to a confidence interval of 95%. The absorbed dose obtained from the air cavity is considered satisfactory due to the insufficient performance of the calculation algorithm used in low density media.

Repeating the whole measurement chain with other dosimeter batches is required using two or three dosimeters in each measurement point for higher precision. However, there was not enough time for more measurements and evaluation within this MSc project during which also the phantom was designed and constructed. Although a virtual phantom measurement with the same dimensions as the calibration phantom was performed, further evaluation measurements can be performed by using simple homogenous phantoms that also undergo the whole treatment chain but are planned for irradiation with a reference field. Such a measurement would be good to perform if dosimetric differences between determined and planned doses are detected somewhere. Comparison between the determined and planned doses with calculations by MC simulations as a benchmark would also be valuable.

The present project will continue for two years as a regional dose audit project between Linköping, Jönköping, Eskilstuna and Kalmar, and further investigation and measurements will be performed.
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48


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