A SYSTEM FOR MAILED DOSE AUDIT IN RADIOTHERAPY USING LITHIUM FORMATE EPR DOSIMETRY

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Abstract

A mailed audit system for dose verification using lithium formate electron paramagnetic resonance dosimetry was designed and evaluated. For this purpose, a semi-anthropomorphic phantom was manufactured, inserted with pellet shaped lithium formate dosimeters and treated with an intensity modulated radiotherapy plan. The measurement results agreed with the planned doses within the estimated standard uncertainties.

1. INTRODUCTION

The aim of radiation therapy is to deliver high doses to the target to achieve local tumour control while protecting the surrounding healthy tissue. The dose needed for local control and the dose tolerated by healthy tissue give a narrow therapeutic window [1, 2]. Therefore, high accuracy in the delivered dose is critical. As radiation therapy techniques are becoming more advanced, quality assurance of machines, delivery techniques and clinical routines become more important. The absorbed dose given in external radiation treatments is related to measurements for determination of absorbed dose to water under reference

conditions using a calibrated ionization chamber traceable to a standard laboratory [3]. When delivering a radiation treatment several factors, other than accelerator output in reference conditions, contribute to the uncertainties in the dose delivered to the tumour and healthy tissue. Therefore, an effective audit system where influences from the whole treatment chain are taken into account, from computed tomography (CT) scanning to contouring of structures, treatment planning and treatment delivery, would be of great value.

There are systems for dose audits for the whole treatment chain or parts of it utilizing anthropomorphic or multipurpose phantoms and thermoluminescent (TL) dosimetry [4–6]. The aim of the present work is to design and evaluate a mailed dosimetry audit system where influences from the whole treatment chain are taken into account, using EPR dosimetry with lithium formate. Experimental details are found in an MSc thesis by Malke [7]. The strategy was to let a phantom undergo the treatment chain for intensity modulated radiotherapy (IMRT) treatment and perform measurements in the phantom to evaluate the dose in relevant points. For this purpose, an audit phantom was designed to be relevant for the head-and-neck region with target and organs at risk (OARs) and inserts for electron paramagnetic resonance (EPR) dosimeters. Point doses in the target and OARs were determined and results compared to planned doses. The IMRT treatment was delivered to the audit phantom using dynamic multileaf collimator technique. All doses stated in this work refer to absorbed dose to water in the medium. This is also valid for the dose values obtained from the treatment planning system.

EPR dosimetry is a method available today with the potential to become a complement to TL dosimetry, which has been used for clinical applications for many years with its advantages of high sensitivity, dosimeter reusability and low energy dependence. However, most TL materials show a supralinearity in the dose response, typically for doses above 1 Gy. Within EPR dosimetry, most dosimeter materials have a linear dose response over a very large dose range. EPR dosimetry with alanine is accepted as a standard dosimetry method, especially for measurements of high doses for industrial applications. Alanine is nearly water equivalent [8] with a lower energy dependence than the common TL dosimetry material lithium fluoride, but has a low sensitivity, which is a drawback for its usefulness in radiotherapy applications [9].

Polycrystalline lithium formate monohydrate (HCO_2LiH_2O — referred to as 'lithium formate') [10] is 2–6 times more sensitive than alanine (depending on read out procedure) and exhibits no zero-dose signal. The dose response is linear for doses up to 1000 Gy. This gives a wide measurement dose range, which facilitates simultaneous measurements in points corresponding to both OARs and target. The readout of the dosimeters is performed with an EPR spectrometer and is non-destructive to the signal, which allows for several readouts to improve the

statistics. Lithium formate is even more water equivalent than alanine regarding mass energy absorption coefficient and mass collision stopping power. The dosimeters used in this study contain 10% paraffin and 90% lithium formate, and have a density of 1.32 g/cm^3. The response of the dosimeters is independent of the dose rate and the beam quality in the ranges that are relevant for the accelerator produced high energy photon beams [11].

In an earlier study [11], no significant signal fading (instability of the radiation induced radicals over time) was found during the first 28 d. However, experiences from several investigations indicate that the fading properties of lithium formate are complex, requiring controlled readout and storing conditions regarding temperature and air humidity. For alanine, the signal dependence of the read out temperature is 0.135–0.190% per K for doses between 20–100 kGy [12]. To the authors' knowledge, there are no published investigations of a possible temperature and humidity dependence for lithium formate, but it is likely that lithium formate has a readout temperature dependency of the same order of magnitude as alanine. There is a concern for how the dosimeters are 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. Lithium formate is also mildly hygroscopic at high air humidities. This has a significant influence on the signal stability at relative humidities above 55–60%. An air tight encapsulation during storage is therefore essential.

Nevertheless, in this work, all irradiations including calibration were performed on one day and all readouts were performed two days later, which made the results insensitive to fading. Before the system is used for a mailed dose audit, the signal fading due to temperature and humidity will be further investigated in order to find routines and corrections to minimize its influence.

Lithium formate has already been used for clinical applications such as pretreatment IMRT verification [11], high dose rate brachytherapy [13] and stereotactic radiosurgery [14]. Since the dosimeters are useful for a wide dose range and are expected to have a stable signal under controlled conditions, it should be a well suited system for mailed dosimetry audits.

2. MATERIALS AND METHODS

2.1. Phantom and dosimeters

An anthropomorphic phantom (Fig. 1) was designed and constructed at Linköping University Hospital after an idea derived from an IMRT phantom designed for a remote monitoring programme [4]. The cylindrical phantom has a diameter of 20 cm and a length of 24 cm. For manufacturing reasons, it consists

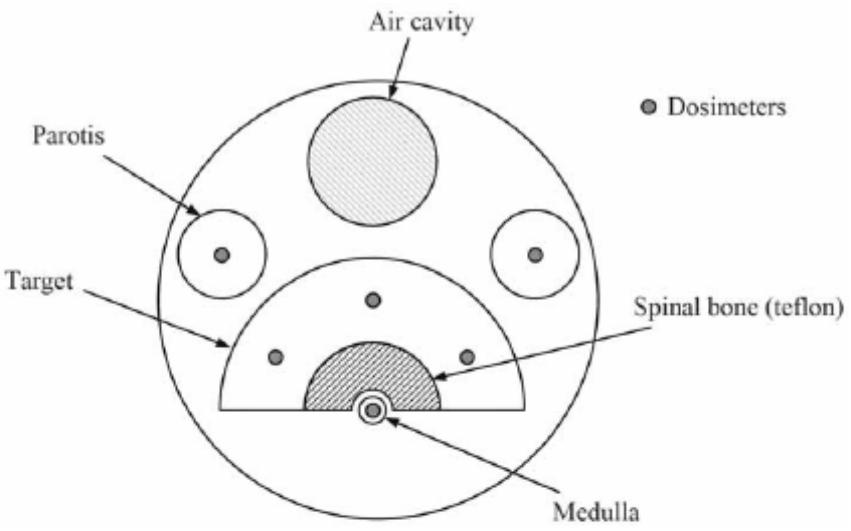

FIG 1. A transversal slice of the audit phantom.

of eight slices tacked together with three rods throughout the phantom. The first and the last slices rest on braces.

The inside of the phantom was designed to mimic the head-and-neck region with the tumour (target) partially encompassing the medulla (OAR). Other OARs are the salivary glands adjacent to the tumour. PMMA (polymethyl methacrylate) was the choice of material since it is near tissue equivalent and readily available. A structure made of Teflon resembling the spinal bones and an inhomogeneity in the form of an air cavity were also included. The air cavity was also treated as an OAR corresponding to lung tissue or trachea. The structures go through the four cylindrical slices in the middle. Three holes were drilled in the target, and one hole each in the salivary glands and the medulla. Cylindrical PMMA tubes with an inner diameter of 5 mm were inserted into the holes for dosimeter placement.

In order to eliminate the dependency on the person contouring the organs, the structures were accommodated to fit tightly in, and to be easily discriminated from, the surrounding material.

The dosimeters were produced with a manual tabletop pellet press following a standardized method [11] giving cylindrical pellets of 5 mm height and 4.5 mm diameter, with a weight of 100 ± 2 mg. The dosimeters consist of 90% lithium formate (Sigma-Aldrich, 98%), which is the active material, and 10% solid household paraffin, which is used as a binder. No encapsulation was needed.

2.2. EPR measurements and readout

A BRUKER EleXsys E 580 spectrometer was utilized for all EPR measurements. The spectrometer was equipped with a standard cavity ER 4102ST. The measured signal is defined as the peak to peak amplitude of the first derivative of the absorption spectrum, divided by the mass of the dosimeter. Every dosimeter was read out five times. In order to reduce uncertainties due to spectrometer response variation over time, the five readings were spread out over the day and the whole batch including calibration dosimeters was read out in one day. The EPR signal was not smoothed, filtered or manipulated in any way and was determined as the mean of all five readings. A quartz glass sample tube with an inner diameter of 5 mm and flat bottom was employed for dosimeter placement in the cavity. 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. For the present work, the spectrometer settings in Table 1 were used.

2.3. Dosimeter batch quality control

It is important to check that all dosimeters respond equally to radiation before use. An upper limit for the relative standard deviation of the mean signal of the batch was set to 1%. Dosimeters not fulfilling that condition are excluded from the batch. In this case, the standard deviation of the mean signal was 0.87%.

All dosimeters of the batch were irradiated, ten at a time in a stack, in a cubic PMMA phantom. The dosimeters were irradiated at 7 cm depth in PMMA in a field of area 10 cm × 10 cm at a source–surface distance (SSD) of 100 cm in a 6 MV photon beam using a Varian Clinac 600 C/D linear accelerator. To account for possible inhomogeneities in the radiation field, the dose was given in

TABLE 1. SPECTROMETER SETTINGS

Microwave power:	20 mW
Modulation amplitude:	1.2 mT
Sweep width:	3 mT
Sweep center:	346 mT
Time constant:	327.68 ms
Sweep time:	167.77 s

ten fractions and the dosimeters were translocated in the stack after each fraction. Thus, the dosimeters were given a total dose of 3 Gy. The signal corresponding to this dose is considered as the background signal, *b*, of the batch.

2.4. Measurements

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

The audit phantom was CT scanned using a Siemens SOMATOM Sensation Open. During the scan, the dosimeters were replaced with PMMA inserts to avoid measuring the dose from the CT scan. The treatment planning system (TPS) used for contouring the phantom structures, and optimizing and calculating the IMRT treatment plan was Helios/Eclipse (Varian) with AAA (analytical anisotropic algorithm). The resulting treatment plan consisted of seven coplanar beams separated by 51–52°. Six EPR dosimeters were placed in the phantom, one in each parotis and the medulla, and three in the target. The phantom was irradiated according to the IMRT treatment plan giving the target a dose of 5 Gy. The absorbed doses in the different structures of the phantom, determined with EPR dosimetry, were compared to the corresponding planned doses from the TPS.

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. The accelerator output and the attenuation in the treatment table were corrected for in the determination of the planned doses.

Two groups of five dosimeters each were used to establish a calibration curve for the batch according to the method described in earlier studies [11, 13]. 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 readout. Results were compared to doses determined with the ionization chamber. Both the calibration and blind test measurements were performed in a PMMA phantom at a depth of 8 cm, in a 6 MV photon beam with a 10 cm × 10 cm field and an SSD of 100 cm. An NE 2571 ionization chamber with a calibration coefficient traceable to a standards laboratory was used as a reference. To compare the TPS with the measurements in a simple homogeneous set-up, a treatment plan describing the blind test was created on a virtual PMMA phantom with the same dimensions as the calibration phantom.

The fact that the reference conditions are not completely fulfilled, using a PMMA phantom instead of water, were taken into account as an increased uncertainty in the beam quality correction factor. 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 as described for the batch quality control.

3. RESULTS

The results from the blind tests and the audit phantom measurements are presented in Tables 2 and 3, respectively. The relative standard uncertainty of the absorbed dose values determined by ionization chamber measurements was assumed to be 1.5%, and the corresponding value for the planned doses were taken to be 3.1% according to a review by Ahnesjö and Aspradakis [15], where 'future values' with a 2% relative standard uncertainty in the dose calculation

TABLE 2. RESULTS FROM THE BLIND TESTS, COMPARED WITH IONIZATION CHAMBER VALUES AND PLANNED DOSES

	Dose, ion chamber (Gy)	Dose, EPR Gy)	Relative difference, EPR–ion chamber (%)	Dose, TPS (Gy)
Group 1	1.53 ± 0.02	1.51 ± 0.03	–1.2 ± 2.4	1.56 ± 0.05
Group 2	3.58 ± 0.05	3.54 ± 0.07	–1.1 ± 2.4	3.63 ± 0.11
Group 3	7.66 ± 0.15	7.68 ± 0.16	0.3 ± 2.9	7.77 ± 0.24

TABLE 3. RESULTS FROM MEASUREMENTS IN THE AUDIT PHANTOM, COMPARED WITH PLANNED DOSES

	Planned dose (Gy)	Dose, EPR (Gy)	Relative difference (%)
Target 1	5.13 ± 0.15	5.03 ± 0.10	–1.9 ± 3.7
Target 2	4.92 ± 0.15	4.74 ± 0.09	–3.7 ± 3.7
Target 3	5.16 ± 0.15	5.03 ± 0.11	–2.4 ± 3.7
Medulla	2.87 ± 0.09	2.83 ± 0.06	–1.4 ± 3.7
Parotis DX	1.19 ± 0.04	1.21 ± 0.02	1.7 ± 3.5
Parotis SIN	1.21 ± 0.04	1.20 ± 0.02	–0.8 ± 3.5

were assumed to be relevant. The relative differences between EPR and ionization chamber measurements are well below the calculated uncertainties in the EPR measurements. A description of these uncertainty calculations are given in the MSc thesis by Malke [7].

4. CONCLUSIONS

This work shows promising initial results for an audit system where influences from imaging, planning and treatment delivery are taken into account. The present project will continue for two years as a regional dose audit project between three or four clinics, and further investigation and measurements will be performed.

For the blind tests, the doses obtained from the EPR dosimeters agreed with the results obtained from the ionization chamber and from the TPS within the estimated standard uncertainties. The absorbed doses from the audit phantom measurements also agree with the planned doses within the estimated standard uncertainties. The experiment will be repeated using three dosimeters in each measurement point for higher precision.

There are several general recommendations of uncertainty limits in the delivered dose, but according to the IAEA [3], the uncertainty in the delivered absorbed dose to a target volume should be less than ±5%. For audit measurements performed in the reference conditions using TL dosimeters, an agreement within 5% is often considered satisfactory.

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REFERENCES

[1] BRAHME, A., Dosimetric precision requirements in radiation therapy, Acta Radiol. Oncol. **23** (1984) 379.

[2] CHETTY, I.J., et al., Report of the AAPM Task Group No. 105: Issues associated with clinical implementation of Monte Carlo based electron external beam treatment planning, Med. Phys. **34** (2007) 4818.

[3] INTERNATIONAL ATOMIC ENERGY AGENCY, Absorbed Dose Determination in External Beam Radiotherapy: An International Code of Practice for Dosimetry Based on Standards of Absorbed Dose to Water, Technical Reports Series No. 398, IAEA, Vienna (2000).
[4] HAN, Y., et al., Dosimetry in an IMRT phantom designed for a remote monitoring program, Med. Phys. **35** (2008) 2519.
[5] SWINNEN, A., et al., The use of a multi purpose phantom for mailed dosimetry checks of therapeutic photon beams: OPERA, Radiother. Oncol. **64** (2002) 317.
[6] BRIDIER, A., et al., A comparative description of three mulipurpose phantoms (MPP) for external audits of photon beams in radiotherapy: the water MPP, the Umeå MPP and the EC MPP, Radiother. Oncol. **55** (1999) 285.
[7] MALKE, Z., System for dose audit for external radiation therapy based on EPR dosimetry with Lithium Formate, MSc Thesis, Stockholm University, Sweden (2010), (http://su.diva-portal.org/smash/record.jsf?searchId=1&pid=diva2:373798
[8] BERGSTRAND, E.S., et al., An investigation of the photon energy dependence of the EPR alanine dosimetry system, Phys. Med. Biol. **48** (2003) 1753.
[9] NAGY, V., et al., Uncertainties in alanine dosimetry in the therapeutic dose range, Appl. Radiat. Isot. **56** (2002) 917.
[10] VESTAD, T.A., et al., EPR dosimetric properties of formats, Appl. Radiat. Isot. **59** (2003) 181.
[11] GUSTAFSSON, H., et al., Lithium formate EPR dosimetry for verifications of planned dose distributions prior to intensity-modulated radiation therapy, Phys. Med. Biol. **53** (2008) 4667.
[12] NAGY, V., et al., Advancements in accuracy of the alanine dosimetry system. Part 2: The influence of the irradiation temperature, Radiat. Phys. Chem. **57** (2000) 1.
[13] ANTONOVIC, L., et al., Evaluation of a lithium formate EPR dosimetry system for dose measurements around Ir-192 brachytherapy sources, Med. Phys. **23** (2009) 2236.
[14] WALDELAND, E., et al., Dosimetry of stereotactic radiosurgery using lithium formate EPR dosimeters, Phys. Med. Biol. **55** (2010) 2307.
[15] AHNESJÖ, A., ASPRADAKIS, M.M., Dose calculations for external photon beams in radiotherapy, Phys.Med.Biol **44** (1999) R99.