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In vivo dosimetry in ^{60}Co teletherapy using electron paramagnetic resonance in L-alanine

Katarzyna Ewa Schultka[1], Bartłomiej Ciesielski[1], Piotr Szewczyk[2]

Objectives. The aim of this study was to evaluate the accuracy of doses absorbed during teletherapy with ^{60}Co beams by comparing them with doses calculated by the radiotherapy treatment planning system.
Materials and methods. The doses were measured in vivo using electron paramagnetic resonance (EPR) in L-alanine. This method of dosimetry is based on the detection of free radicals generated by ionizing radiation in the dosimetric material which is polycrystalline L-alanine. The concentration of free radicals is proportional to the absorbed dose. The EPR technique allows for determining relative concentrations of the radicals and for calibration of the EPR signal intensity vs. the absorbed dose. The measurement is non-destructive and therefore allows for dosimetry of a single fraction dose, as well as the total dose of radiotherapy using the same detector. The detectors are small polyethylene bags (16 mm x 16 mm x 1.6 mm) filled with crystalline L-alanine powder. Clinical research was performed on a group of patients undergoing radical and palliative treatment at the Department of Oncology and Radiotherapy of the Medical University of Gdansk.
Results. The entry dose was measured for 72 fields irradiated by ^{60}Co photons localized within the head and neck, the chest and the pelvis. The accuracy of the EPR dosimetry was about 3% (one standard deviation) for doses above 2 Gy. The results of in vivo dosimetry were compared with doses calculated by radiotherapy treatment planning systems. The average deviation of the measured doses from doses obtained during planning was 0.21%, with a data scatter of 3.5% (standard deviation for a single measurement). A detailed procedure of the developed dosimetric method is presented.
Conclusions. The results of in vivo dosimetry show good correlation between the prescribed and the actually delivered doses. The 0.21% average difference can be accounted as satisfactory in routine radiotherapy treatments. The sources of four measurement errors exceeding 10% were investigated and explained.

Dozymetria *in vivo* w teleterapii ^{60}Co z wykorzystaniem elektronowego rezonansu paramagnetycznego w L-alaninie

Cel pracy. Celem pracy była ocena dokładności dawek promieniowania podczas teleterapii nowotworów z wykorzystaniem ^{60}Co poprzez porównanie dawek zmierzonych in vivo z dawkami obliczonymi przez komputerowe systemy planowania.
Materiały i metody. Pomiarów in vivo dokonano metodą spektroskopii elektronowego rezonansu paramagnetycznego (EPR) w L-alaninie. Metoda ta polega na detekcji stabilnych wolnych rodników generowanych przez promieniowanie jonizujące w materiale dozymetru. Stężenie wolnych rodników w alaninie jest proporcjonalne do pochłoniętej dawki promieniowania, a amplituda ich sygnału EPR może być wykalibrowana w zależności od pochłoniętej dawki. Zaletą tej metody jest nieniszczący sposób pomiaru, umożliwiający zarówno pomiar dawki frakcyjnej, jak i dawki całkowitej przy użyciu tego samego detektora. Badania kliniczne obejmowały grupę pacjentów leczonych radykalnie i paliatywnie w Katedrze i Klinice Onkologii i Radioterapii Akademii Medycznej w Gdańsku.
Wyniki. Zmierzono dawkę wejściową dla 72 pól napromieniowanych fotonami ^{60}Co. Pola obejmowały okolice głowy i szyi, klatki piersiowej oraz miednicy. Zastosowano dozymetry alaninowe w postaci niewielkich (16 mm x 16 mm x 1,6 mm) saszetek polietylenowych, wypełnionych sproszkowaną krystaliczną L-alaniną. Dokładność pomiarów EPR wynosiła ok. 3% (jedno odchylenie standardowe) dla dawek powyżej 2 Gy. Porównano wyniki pomiarów in vivo z wartościami dawki planowanej przez komputerowe systemy planowania. Średnie odchylenie dawki zmierzonej od zaplanowanej wynosiło 0,21%, z rozrzutem 3,5% (odchylenie standardowe pojedynczego pomiaru).
Wnioski. Uzyskane wyniki wykazały zgodność między dawkami zmierzonymi a obliczonymi. Średnie odchylenie pomiędzy obydwiema dawkami na poziomie 0,21% można uznać za zadowalające dla rutynowo prowadzonej radioterapii. Dla

[1] Department of Physics and Biophysics
[2] Department of Oncology and Radiotherapy
Medical University of Gdańsk, Poland

czterech przypadków, w których uzyskano ponad 10% rozbieżności dawki zmierzonej od zaplanowanej, przeprowadzono analizę przyczyn tych niezgodności.

Key words: alanine, EPR, dosimetry, radiotherapy, ^{60}Co
Słowa kluczowe: alanina, EPR, dozymetria, radioterapia, ^{60}Co

Introduction

Unity of the planned and actually delivered dose is an essential issue in radiotherapy and determines the final therapeutic effect of the treatment. Discrepancies between prescribed and delivered doses may increase the risk of complications in case of overdosing, or reduce the tumor control probability in case of underdosing. According to ICRU and WHO recommendations [1, 2], the acceptable difference between the delivered and planned dose is 5%. Such accuracy requires individual treatment planning and verification of the calculated doses by direct *in vivo* measurements.

In vivo dosimetry, which enables a regular control of fraction doses, allows for necessary corrections during radiotherapy. Currently, semiconductor probes or thermoluminescence detectors are most widely used for routine *in vivo* dosimetry. An alternative dosimetric method is electron paramagnetic resonance (EPR) spectroscopy using L-alanine as the detector material. This method is based on detection of stable free radicals, which are generated in L-alanine by ionizing radiation. The dominant stable radical in room temperature is CH_3CH^*COOH, which is created through deamination of the alanine molecule. The concentration of free radicals depends on the absorbed radiation energy. Thus, the intensity of the EPR signal is a measure of dose. In conditions of constant line width of the EPR spectra, which for alanine occurs in a broad dose range [3], amplitude of the central line of the spectrum (Figure 1) is commonly used as a measure of the absorbed dose. Especially in case of weak, low-dose noisy signals, this method surpasses assessments based on a double integral of the spectrum [4]. The EPR/alanine dosimetry was introduced in the early 1980s for the measurement of medium and high doses [5]. More recently, the applications of this dosimetric method for measurements of spatial dose distribution for high-energy photon and electron beams in teletherapy [6-8] were reported. This method was also successfully used to monitor single fraction radiotherapy doses [9-12]. Currently available EPR spectrometers allow for accurate dose measurements at levels below 1 Gy [13].

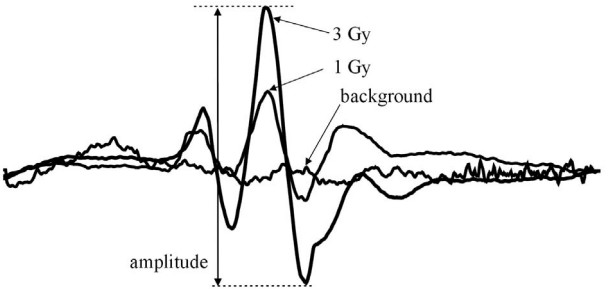

Figure 1. EPR spectra of L-alanine irradiated with doses typical for a single fraction (0.5-3 Gy)

Stability of the dosimetric signal, broad range of linear response to a dose up to ~10 kGy and nondestructive readout permit for measuring the total, accumulated dose during the whole treatment. One of the important advantages of this method is its flat energy response above 150 keV and similar sensitivity to photons and electrons [6-7]. This feature provides the unique possibility of measuring the total dose in mixed photon/electron beam radiotherapy with one detector.

Material and methods

Polycrystalline, fine-powdered L-alanine (SIGMA Chemical Company) was used as a detector material. The detectors had a form of small (1.6 cm x 1.6 cm x 1.6 mm) polyethylene bags filled with 0.5 g of alanine powder. The source of ^{60}Co radiation was the Theratron 780C, AECL. Detectors were placed in the middle of the radiation field and directly taped either to the skin (in chest and pelvis cancer treatment) or to the mask (in head and neck cancer treatment), as shown in Figure 2. All detectors were covered by 5 mm layer of polymethyl metacrylate (PMMA) to ensure electron equilibrium conditions. The measured doses were compared with doses at D_{max} calculated by a radiotherapy treatment planning (RTP) system – the CadPlan R.3.1.2. (Varian INC.). The small decrease in SSD for the detector (Figure 2) was taken into account in the conversion of

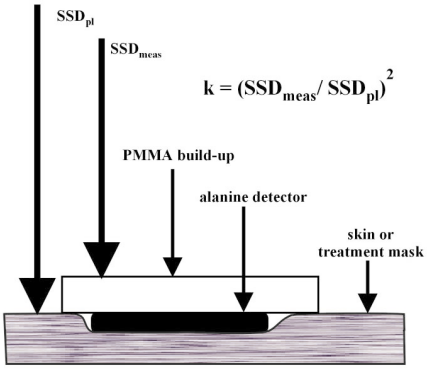

Figure 2. A procedure for calculating of correction factor *k* accounting for a change of SSD for the applied detectors

the planned "in-tissue doses" to "detector doses". After the irradiation, the alanine powder was transferred into EPR quartz tubes and the dosimetric signal was measured with a Varian E-4 spectrometer at 5 mW microwave power, 1.25 mT modulation amplitude. These spectrometer parameters were previously determined as giving the optimal signal-to-noise ratio [9-10]. All readings were normalized with regard to the linear packing density (d) of powder inside the quartz tube and the spectrometer gain (G), according to the following formula:

$$I = \frac{A}{G \cdot d} \quad (1)$$

where A stands for amplitude of the central EPR line (Figure 1) and I is the normalized signal amplitude.

The efficiency of free radicals generation depends on the actual temperature of the detector during irradiation [14]. Because the detectors located on skin differed in temperature from those applied during calibration procedure (performed at 23°C), these temperature differences were taken into account by introducing a temperature correction factor k(T). Due to variations of the detector temperature during the 1-4 minute irradiation sessions, a time-averaged correction factor was calculated according to the formula:

$$\bar{k}(\tau) = \frac{1}{\tau} \int_0^{\tau} k(t)dt \quad (2)$$

where τ stands for time of irradiation and k(t) is a function describing dependence of the correction factor on duration of the detector contact with the skin. This function is shown by the solid line in Figure 3. It was calculated by taking an average between temperatures measured by thermocouples located above and below the alanine detector taped to patient's skin.

The temperature corrected intensities of the EPR signals were converted to dose using a standard alanine sample of 72 Gy. The linear response of the dosimetric EPR signals in this dose range was demonstrated in our previous reports [9-10].

The detectors were applied to patients who were administered radical and palliative radiotherapy at the Department of Oncology and Radiotherapy of the Medical University of Gdansk, and EPR measurements were performed at the Department of Physics and Biophysics.

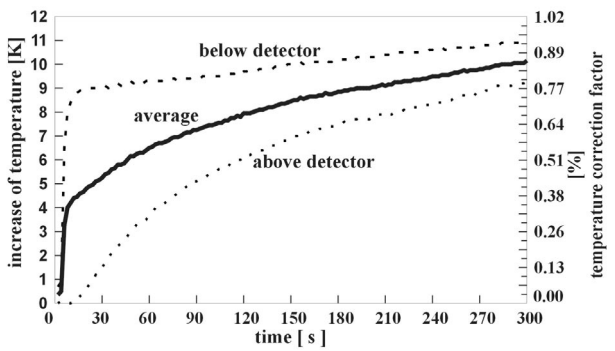

Figure 3. Temperature correction factor necessary because of detector warming brought on by contact with patient's skin. The dashed lines show temperature variations measured above and below the detector. The solid line presents the k(t) function applied in eq. (2) to calculate the temperature correction factor averaged over irradiation time

Results

The *in vivo* measurements were performed in a total of 72 therapeutic fields (40 in the head and neck region, 12 in the supraclavicular region, 15 over the chest and 5 over the pelvis. The results are presented in fig. 4, where solid lines show theoretically determined margins of EPR measurement error, including electronic noise, reproducibility of the spectrometer parameters and background line fluctuation. The triangles show the differences [%] between the doses measured *in vivo* and calculated by RTP. In fig. 5 the differences are presented as a histogram. The average difference between the measured and calculated doses was +0.2%, the standard deviation of a single measurement was 5.3%.

Discussion

Our results show that the recommended 5% limit in accuracy of dose delivery can be verified by means of EPR/alanine dosimetry in the range of doses typical for a single radiotherapy fraction. To the best of our knowledge, no similar dose measurements using this method as *in vivo* clinical practice have yet been reported by other authors. This dosimetric method hardly affects the treatment course – a shift in isodose distribution is about 5 mm, only in the field region below the detector. The application of the detector elongates the time during which the patient occupies the therapeutic table by about 10 sec.

Ex post analysis of four cases with deviations from prescribed dose which had exceeded 10% (the points marked with arrows in Figures 4 and 5) resulted in identification of the sources of these deviations. They resulted from errors in the irradiation procedure after

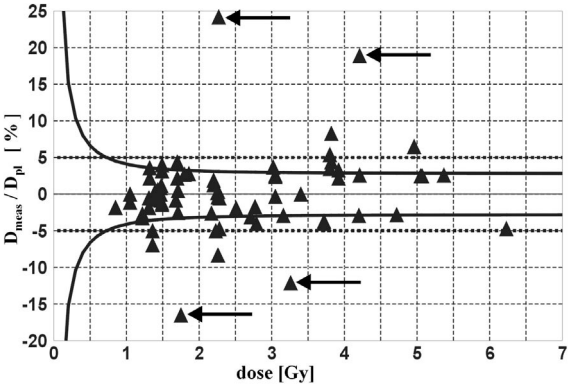

Figure 4. Percentage differences between the doses measured and planned. The solid lines mark the calculated EPR measurement uncertainty. The dotted line shows the ±5% margin recommended by ICRU

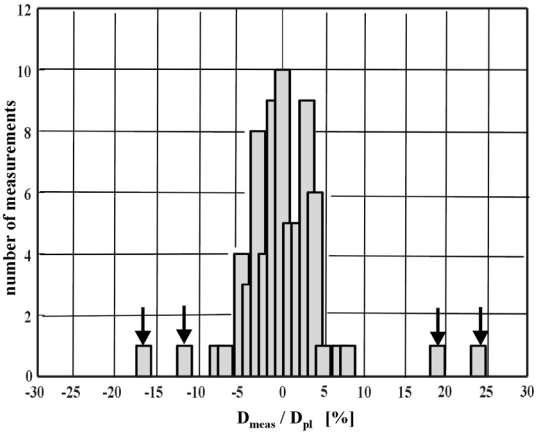

Figure 5. Histogram of percentage differences between doses measured and planned

changes in SSD values, which were introduced during the treatment. After excluding the four erroneous results from the analyzed data, the standard deviation of a single measurement decreased from 5% to 3.5%. The low value of mean deviation of measured doses from calculated doses (0.2 %) supports the conclusion that no systematic errors (in source calibration, treatment planning procedure, technical aspects of patient positioning etc.) occurred during the treatment.

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Katarzyna Ewa Schultka M.Sc.
Medical University of Gdańsk
ul. Dębinki 1, 80-211 Gdańsk, Poland
e-mail: kschult@amg.gda.pl

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