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In vivo dosimetry using electron paramagnetic resonance in L-alanine in gynecological low dose rate brachytherapy

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Objectives. to present the results of in vivo dosimetry performed on 15 patients treated for gynecological cancer with the aim of optimizing the detector design and its application in body cavites and comparing the doses measured in vivo with those calculated by the Plato (Nucletron) system of brachytherapy treatment planning.
Material and methods. Electron paramagnetic resonance (EPR) is, as a dosimetric method, based on the detection of free radicals generated by ionizing radiation in L-alanine. The concentration of free radicals is proportional to the absorbed dose and is determined by the EPR technique. The detectors appear as small cellulose capsules (outer diameter 5 mm, length 15 mm), tightly filled with crystalline L-alanine powder. The doses from ^{137}Cs brachytherapy sources were measured in selected points inside the rectum and vagina.
Results. The relative deviations of measured doses from those calculated by the treatment planning system ranged from -28% to +40%. The mean deviations from the prescribed doses were relatively low (+1% for detectors placed in the rectum, – 10% for detectors placed in the vagina). However, due to a low number of samples and large standard deviations of the mean values (±23% and ±11% for detectors placed in the rectum and the vagina, respectively), the deviations of the mean values are of low statistical significance. The accuracy of the measurements was analyzed and is hereby discussed.
Conclusions. The main sources of the differences between the measured and calculated dose should, generally, be attributed to uncertainties in the determination of the detector position inside the body as ascertained from the radiographs and to uncontrollable motion of detectors during treatment.

Dozymetria *in vivo* metodą spektroskopii EPR alaniny w brachyterapii ginekologicznej

Cel. W pracy przedstawiono użycie dozymetrii in vivo metodą spektroskopii elektronowego rezonansu paramagnetycznego (EPR) L-alaniny w brachyterapii ginekologicznej oraz optymalizację budowy detektorów i ich umieszczania we wnękach ciała pacjentki.
Materiały i metody. Technika EPR oparta jest na wykrywaniu stabilnych wolnych rodników wytwarzanych przez promieniowanie jonizujące w materiale dozymetru. Liczba rodników generowana w jednostce masy detektora jest proporcjonalna do pochłoniętej dawki promieniowania. Zastosowano dozymetry alaninowe w postaci kapsułek o średnicy zewnętrznej 5 mm i długości 15 mm, wypełnionych sproszkowaną krystaliczną L-alaniną. Wyniki pomiarów in vivo porównano z wartościami dawki obliczonej za pomocą systemu planowania PLATO firmy Nucletron.
Wyniki. Rozbieżności pomiędzy dawkami planowanymi i zmierzonymi zawarte były w granicach od -28% do +40%. Średnie odchylenie było niewielkie (+1% dla detektorów umieszczonych w odbytnicy, -10% dla detektorów umieszczonych w pochwie), jednakże z powodu małej ilości próbek i stosunkowo wysokiego odchylenia standardowego (odpowiednio ±23% i ±11% dla detektorów umieszczonych w odbytnicy i w pochwie) odchylenia średnich wartości nie są istotną statystycznie miarą zgodności pomiędzy dawkami zmierzonymi a obliczonymi.
Wnioski. Za główną przyczynę rozbieżności pomiędzy dawką zmierzoną i obliczoną uznano niepewność określenia położenia detektorów wewnątrz ciała i ich przemieszczanie się w czasie trwania terapii.

Key words: alanine, EPR, dosimetry, brachytherapy, ^{137}Cs
Słowa kluczowe: alanina, EPR, dozymetria, brachyterapia, ^{137}Cs

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Introduction

The effect of radiotherapy depends on the precision of delivery of the prescribed dose to the target volume. The accuracy of dose delivery is a crucial issue in radiotherapy. The difference between planned and actually delivered doses may decrease the probability of tumor control or increase the risk of post-radiation complications. In gynecologic brachytherapy the critical organs include the rectum and the urinary bladder. Late complications from these two organs may significantly decrease the patients' quality of life. The International Commission on Radiation Units and Measurements (ICRU) recommended the use of a 60% isodose as the reference target volume for intracavitary therapy in gynecological cancer [1].

One of the dosimetric methods used both in teletherapy [2-7] and brachytherapy [8-10] is EPR/alanine dosimetry. The advantages of the alanine detector include water equivalence, flat energy dependence and non-destructive readout. We have recently published a feasibility study on applications of EPR/alanine dosimetry in external beam radiotherapy [5]. In the present study we present our preliminary results of *in vivo* measurements using EPR/alanine dosimetry in gynecologic brachytherapy.

Material and methods

The detectors were applied in 15 gynecological cancer patients (7 cases of cervical cancer and 8 cases of endometrial cancer) treated with low-dose rate (LDR) brachytherapy (Selectron, Nucletron, The Netherlands) in the Department of Oncology and Radiotherapy, Medical University of Gdansk (MUG). Three patients were treated with definite irradiation and 12 patients underwent postoperative radiotherapy. In all fifteen cases only vaginal ovoids were employed. The dose distribution in the pelvic region was calculated with a computer planning system (PLATO – Nucletron, The Netherlands) after applicator insertion. The positions of the detectors (placed in the rectum and in the vagina) were determined using AP and lateral orthogonal radiographs. The Selectron LDR/MDR (Nucletron, The Netherlands) afterloading radiation system containing ^{137}Cs sources was used in all cases.

The detectors had a form of small cellulose capsules (external diameter 5 mm; length 15 mm) filled with 0.5 g of alanine powder (SIGMA Chemical Company). The capsules were sealed in waterproof Parafilm pockets.

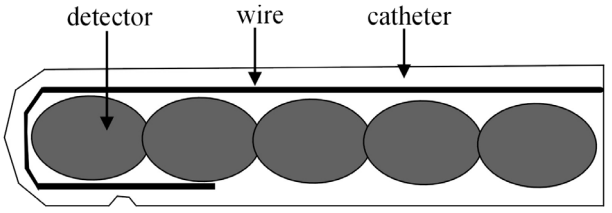

Figure 1. A schematic diagram of detectors placed inside Foley's catheter

Three methods of detector application were used in this study. In the first, the detectors replaced a flexible lead wire one marker inserted into the rectum. Six alanine detectors were placed in the main channel of a Foley's catheter. Inside the second, thinner channel a lead wire (1 mm in diameter) was placed in order to visualize the catheter on radiographs (Figure 1). The catheter was then sealed in a 0.2 mm thick waterproof polyethylene foil and placed in the rectum (instead of the routinely used lead wire marker – Figure 3). The other two methods were used for *in vivo* dosimetry within the vagina. In the second method, the capsules sealed in waterproof foil were wrapped around with a few coils of radio-opaque thread and then placed in the vagina (Figure 2a). The third application method used capsules fitted to an oval frame made of 1 mm steel (Figure 2b). The capsules with the steel frame were sealed in a waterproof foil pocket and placed in the vagina after the ovoid application.

The doses were calculated at the center of the dosimeter with a computer planning system. The geometry of the detector position was reconstructed from two orthogonal radiographs.

EPR measurements were performed in the Department of Physics and Biophysics of the MUG. After irradiation, the alanine powder was transferred into an EPR quartz tube 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 [4-5]. All readings were normalized with regard to spectrometer gain and linear packing density of powder inside the quartz tube [4-5].

The efficiency of free radicals generation depends on the temperature during irradiation [11]. Because the temperature of the detectors located inside the body cavities differed from the temperature used during the calibration procedure (performed at 23°C) a temperature correction factor k(T) calculated according to data of Nagy et al. [11] was introduced. The temperature corrected intensities of the EPR signals were converted to dose using a reference alanine sample irradiated with ^{60}Co to the dose of 72 Gy. The linear response of the dosimetric EPR signal in this dose range was demonstrated in our previous reports [4-5]. Given the difference in the radiation quality between the *in vivo* irradiated detectors (662 keV γ rays) and the reference alanine sample (1.25 MeV γ rays), a correc-

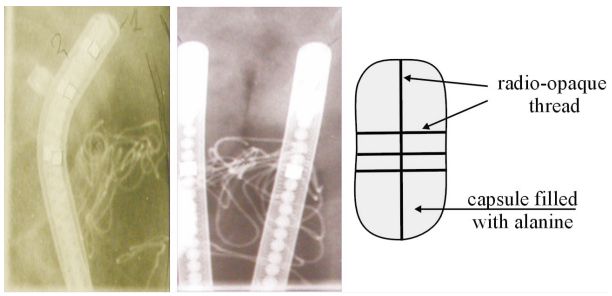

Figure 2a

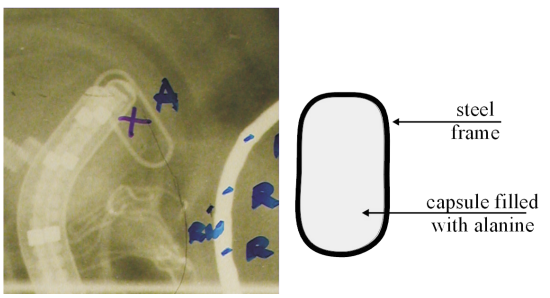

Figure 2b

Figure 2. Radiographs of detectors placed in the vagina. The diagrams beside the radiographs show the placement of the radio-opaque thread (Figure 2a) and the steel frame (Figure 2b), which allow to localize the detectors on the radiographs

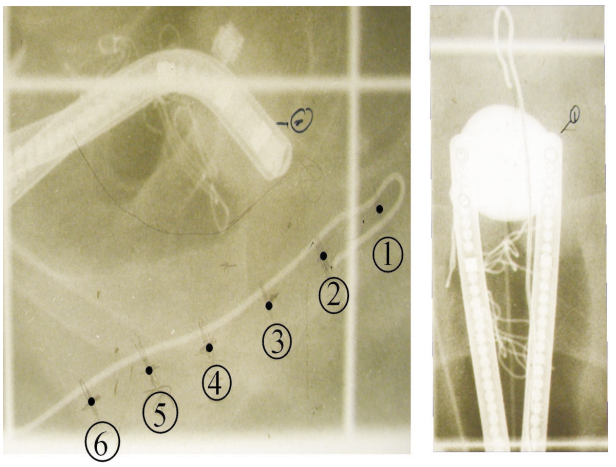

Figure 3. Radiographs with detectors placed in the rectum. Black points indicate the localization of the center of the detector

tion factor accounting for differences in mass absorption coefficients at those two energies [12] was additionally introduced in the dose calculations.

Results

The differences between the measured and the calculated doses for all three application methods are given in Table I. For the six detectors placed in the rectum the differences between the measured and the planned doses varied from -25% to +40%, depending on the localization of the dosimeters. For the eight patients who had detectors with radio-opaque thread placed in the vagina, the differences varied between -28% and -1%. For doses measured using detectors with a steel frame the deviations varied from -23% to 14%. The third method (with steel-frame detectors) resulted in the best visualization of the detectors on radiographs, as shown in Figures 2 and 3.

Discussion

Detectors used for *in vivo* dosimetry should not interfere with the therapeutic process. In addition, the detector should be well visualized on radiographs and should maintain stable position during the planning process and treatment delivery. Our results of *in vivo* dosimetry in the rectum (samples no. 1-6 in Table I) show certain systematic differences between the measured and the planned doses. These differences can be explained by a shift in catheter position during treatment delivery from its original location assumed for dose calculations, i.e. the rotation of the whole catheter in such a way, that the detectors no. 2 and 3 were shifted towards the applicator and detectors no. 5 and 6 moved away from the applicator (Figure 3). This change in positions might have been caused by intestinal movements and involuntary patient movements.

Of the three methods used in this study, two were used only for *in vivo* dosimetry in the vagina. The radio-opaque thread did not allow for a precise determination of detector position – mainly due to the poor quality of the radiographs used for the verification of their locations in the vagina. The use of "steel-frame detectors" (the third method of application) caused a significant improvement in the precise localization of detectors on radiographs. However, this did not offer considerable improvement in the difference between the planned and the measured dose. In our previous studies using EPR/alanine dosimetry in external beam radiotherapy [4-5] errors of the EPR signal measurements reached approximately 2-3% for doses at the level of a few Gy. Therefore, the much greater differences demonstrated here for dosimetry in brachytherapy cannot be attributed to the uncertainty of EPR measurements or to the determination of actual dose absorbed in the detectors.

Table I. Results of *in vivo* dosimetry in the rectum and in the vagina using three methods of application of the detectors. The method of detector visualization on the radiographs is given in the last column. The sample numbers (column 2) refer to their positions shown in Figure 3. D_{meas} and D_{pl} stand for measured and planned dose, respectively. ROT denotes data obtained in detectors with radio-opaque thread, and SF denotes detectors in a steel frame

Case	Sample number	Planned dose [Gy]	$(D_{meas} - D_{pl})/ D_{pl}$	Visualization method
1	1	9.7	0%	catheter
1	2	15.7	40%	catheter
1	3	15.2	15%	catheter
1	4	10.1	-6%	catheter
1	5	6.8	-25%	catheter
1	6	4.2	-16%	catheter
2		29.2	-4%	ROT
3		30.0	-4%	ROT
4		31.4	-1%	ROT
5		43.5	-8%	ROT
6		44.5	-24%	ROT
7		45.7	-9%	ROT
8		45.7	-28%	ROT
9		56.1	-7%	ROT
10		15.7	-23%	SF
11		16.8	-9%	SF
12		25.0	14%	SF
13		38.9	-7%	SF
14		46.0	-18%	SF
15		62.7	-16%	SF

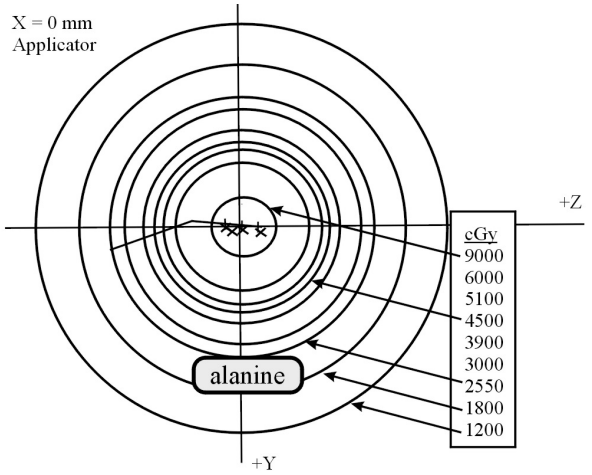

Figure 4. Contours of the alanine detector on the top of an exemplary isodose distribution. The arrows indicate isodoses appropriate to selected doses given in the frame

The main source of the observed discrepancies seems to be related to two factors. The first one is the uncertain three-dimensional localization of the detectors within the body, and the other – the steep gradient of doses typical for brachytherapy, which causes significant changes in the readout doses with small deviations of the assumed vs. actual position of the measurement point. For example, the shift in the detector position of approx. 1 mm, which is plausible in the *in vivo* conditions, may cause a change in the dose readout ranging from 10% to 20% (depending on particular isodose distribution and detector location).

In addition, the errors can vary with the detector size and its orientation (parallel or orthogonal) with respect to isodose distribution. The dose which was calculated (D_{pl}) using the computerized planning system refers to a point, while the measured dose (D_{meas}) refers to an average value over the entire dosimeter volume. Qualitatively, the importance of this effect is illustrated in Figure 4, in which the detector contour is superimposed on a typical ^{137}Cs spatial isodose distribution.

Preliminary *in vivo* dosimetry results reported by other authors confirm our notion that a precise positioning of the detectors and their size are of paramount importance for the final accuracy of dosimetry [9,10]. The use of smaller alanine detectors (3-4 mm) firmly fixed to the applicator wall [9] or to the patient mould [10] allows for smaller discrepancies between the calculated and the planned doses (up to 10%-13 %) despite a similar precision of the EPR signal readout (2-5%).

Conclusions

Currently, EPR/alanine *in vivo* dosimetry applied for intracavitary brachytherapy allows for only a rough estimate of the actual absorbed dose. The lack of precision in detector localization, usually based on radiographs and unavoidable detector shifts during treatment process are the main causes limiting the accuracy of *in vivo* measurements. Further improvement in the experimental verification of the planned brachytherapy doses can be achieved if the problems of reduction of the dosimeters size and their precise, three dimensional localization are solved. At present, it remains impossible to prevent movements of the detectors inside the body during the several hours of the LDR treatment session.

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