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ALANINE/EPR DOSIMETRY AS A POTENTIAL TOOL FOR QUALITY ASSURANCE IN PROTON BEAM RADIOTHERAPY*

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Abstract. Free-radical, alanine/EPR dosimetry can be applied to measure beam doses and cumulative doses delivered to the target volume in proton beam radiotherapy, as a supplementary part of the Quality Assurance program of the proton ocular radiotherapy procedure at the Institute of Nuclear Physics (IFJ PAN). Development of suitable characteristics of the alanine dosimeter and the principle of application of this detector in proton beam radiotherapy are described.

Key words: alanine, electron paramagnetic resonance, proton radiotherapy, quality assurance system.

1. INTRODUCTION

Alanine dosimetry is a method based on the generation of radiation-induced radicals in the L-α–alanine amino acid (CH_3-$CH(NH_2)$-COOH). The concentration of stable radiation-induced radicals trapped in the crystal structure of alanine is proportional to the absorbed dose over a wide range of doses (1–10^5 Gy) [1]. The concentration of these radicals can be estimated quantitatively using the electron paramagnetic resonance (EPR) spectrometry. The alanine spectrum consists of five spectral lines and the peak-to-peak amplitude of the central line is considered to be the dosimetric signal [2]. As EPR readout of the stable radiation-induced free radical signal does not destroy it, it is possible to measure the dose accumulated in the alanine detector in its consecutive exposures. Thus, it is possible to control, in a cumulative manner, the dose received by the patient in consecutive fractions of the patient's irradiation procedure as an additional element of the Quality Assurance (QA) of the dosimetry chain in the radiotherapy procedure.

At the Institute of Nuclear Physics (IFJ PAN) preliminary studies have been carried out to investigate the possibility of applying alanine as a dosimeter for the

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therapeutic proton beam, for Quality Assurance purposes. Modification of the Bruker ESP 300 spectrometer operating in the microwave X-band to perform quantitative dose measurements was the first step of the project. The EPR spectrometer is now equipped with a glycol-based cooling system which improved its performance and stability. A digital data acquisition module was also developed to facilitate quantitative analysis of the EPR spectra.

2. QUALITY ASSURANCE IN RADIOTHERAPY

Within a quality management system in radiotherapy, Quality Assurance represents the activity concerned with providing the highest accuracy, reliability and repeatability of all radiotherapy procedures. In particular, this refers to the dosimetry system, treatment planning and delivery, and to the performance of the equipment and personnel [3].

One of the key elements of QA in clinical radiotherapy is to achieve the required precision and stability of the dosimetry chain. Dosimetry of the proton beam applied in proton radiotherapy requires additional elements to those usually applied in beams used in conventional radiotherapy with external photon and electron beams. At the Institute of Nuclear Physics of the Polish Academy of Sciences (IFJ PAN) in Krakow, ocular proton radiotherapy with a 60 MeV proton beam is under way [4] and a facility for treating all neoplastic sites using a 230 MeV proton beam, a rotating proton gantry and active Bragg peak spreading technique are under construction. In addition to the dosimetry chain of the proton beams based on ionisation chambers, EPR/alanine dosimetry is also being investigated to supplement the QA of the dosimetry system. The alanine-based dosimetry system will be able to measure cumulatively the total dose received by the patient during the whole treatment (the typical fractionation scheme for treating ocular tumours is 4×15 CGE = 54.55 Gy) and to serve for proton beam dosimetry before each therapeutic irradiation. To successfully apply alanine dosimetry as a routine dosimetry method for proton radiotherapy at IFJ PAN, several steps have to be resolved. The first one involves the selection of an optimum alanine detector (commercially available, or in-house manufactured) in terms of its mechanical stability, radiosensitivity, linearity of dose response etc. In the following steps, dosimetry protocols will need to be developed and verified, describing precisely all procedures performed before, during and after the treatment with regard to the application of alanine dosimetry.

3. MATERIALS AND METHODS

Three different kinds of alanine detectors were investigated: rods (produced by Dr. A. Wieser from Helmholtz Zentrum München), pellets (produced by

Gamma Service, Juri-Gagarin Str. 15, D-01454 Radeberg, Germany) and films [5]. These detectors are of different shapes, dimensions and alanine content. Detectors in the form of rods (4.9 mm in diameter, 10.5 mm height) consist of ca. 95% of crystalline alanine (by weight) and 5% polyethylene (which is the commonly used binding material). The pellet-shaped detectors (4.8 mm in diameter, 3.0 mm height), consist of 96% alanine and 4% of undisclosed binder. Alanine foils consist of 30% alanine powder and 70% polyethylene-vinyl-acetate. Foil detectors were cut into disks after their irradiation (4.9 mm in diameter and 0.25 mm thick) to be placed in the 5 mm diameter quartz sample vessel of the EPR spectrometer.

Irradiation of all tested detectors was performed at IFJ PAN, by:

– 60 MeV protons from the AIC-144 cyclotron beam;

– γ radiation (considered as reference radiation for the proton beam according to the *TRS-398 IAEA* dosimetry protocol [6]) from a Theratron 780E unit with a Co-60 γ-ray source.

EPR measurements were performed using the upgraded Bruker ESP 300 spectrometer, available at IFJ PAN. Alanine read-out parameters were as follows: microwave power 7.93 mW, modulation amplitude 9.77 G, modulation frequency 100 kHz, receiver gain $2 \cdot 10^4$, time constant 327.68 ms, conversion time 20.48 ms, magnetic field resolution 1024 points. Each measurement was performed in accumulating mode: with three sample scans to improve the signal-to-noise ratio.

4. RESULTS

Various properties of alanine as a dosimetric tool have previously been reported: tissue equivalence [7], independence on environmental agents (except for high humidity and intense light exposure) [8], signal stability (low fading) [7] and non-destructive read-out [9].

In this study we discuss some of the main properties of alanine detectors which have been examined at IFJ PAN. Among others, we verified the dose response of alanine over the dose range encountered in proton radiotherapy. Alanine detectors in the form of rods and pellets were irradiated in the centre of the spread-out Bragg peak (range in water 29.3 mm, full modulation), which is the measurement reference depth according to the TRS-398 protocol. Detectors were irradiated over the range of doses 1–70 Gy, as determined by a Markus ionisation chamber. The results are shown in Fig. 1. The tested detectors show good linearity over the above dose range (in both cases the correlation coefficient, $R \approx 1$). In practice these calibration curves are used for dose determination in alanine dosimetry. For rod and pellet alanine detectors the lowest limit of detection (LLD) has been set at 1 Gy (with total uncertainty of dose determination at 1 Gy of 18.84% for rods and 12.14% for pellets). Original results obtained for rods have already been published [10].

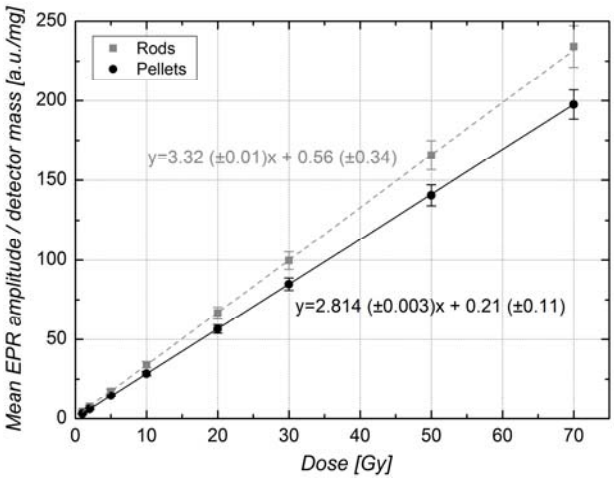

Fig. 1 – Calibration curves obtained for alanine detectors in the form of rods or pellets. Alanine detectors were irradiated at the centre of the spread-out Bragg peak of a 60 MeV proton beam.

Alanine foil detectors do not show sufficient sensitivity over the range of doses applied in radiotherapy. A detectable EPR signal was observed in the examined alanine foils at doses exceeding 150 Gy, however, to obtain a reproducible signal the required dose was 250 Gy [10]. Using a calibration curve (determined over the range 250–1500 Gy for this study), alanine foils (due to their thickness of 0.25 mm) can be used in tests requiring high spatial resolution, such as establishing the relative effectiveness of alanine over particular regions of the Bragg curve where large variation of LET (Linear Energy Transfer) is observed. Results of these measurements have already been reported [10]. We had concluded that no significant difference in alanine response after irradiation by protons within the energy range 57.8–4.5 MeV (SRIM calculations), relative to γ-ray doses, is observed. Our present results confirm this conclusion: as shown in Fig. 2, for an alanine pellet placed at the centre of the spread-out Bragg peak, the dose value, as read out from the alanine detector, is equal to that from exposure to an equal dose of reference radiation (Co-60 γ -rays).

Currently we are developing our own methods of producing alanine pellets, using microcrystalline cellulose as a binder for alanine powder [11]. We are examining the alanine concentration, mass and size of the pellet and applied compression conditions in order to achieve optimum dosimetric and mechanical properties of our detectors. In our first attempt, our in-house produced pellets, of 4.6 mm diameter and height between 2.9 mm and 3.2 mm, had different alanine contents by weight: 70%, 80% and 90%. The preliminary calibration curves obtained over the range 1-10 Gy (irradiated with the Co-60 γ-ray source) for self-manufactured detectors in comparison to previously examined Gamma Service pellets are presented in Fig. 3. As expected, the highest signal is observed for the

Gamma Service detectors containing 96% of alanine and for our detectors containing 90% of alanine. However, due to the poor mechanical stability of our 90% alanine pellets, we may find those containing 80% of alanine to be more suitable for use in routine practice. Our work on manufacturing alanine detectors is in progress.

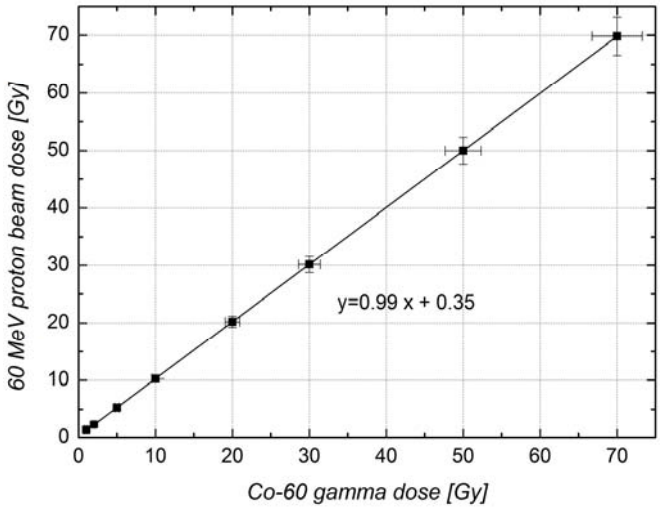

Fig. 2 – The dose response of a pellet alanine detector placed in the centre of a modulated 60 MeV proton beam *vs*. its response to doses of reference radiation (Co-60 γ-rays). The uncertainties of linear fit are considered to be insignificant.

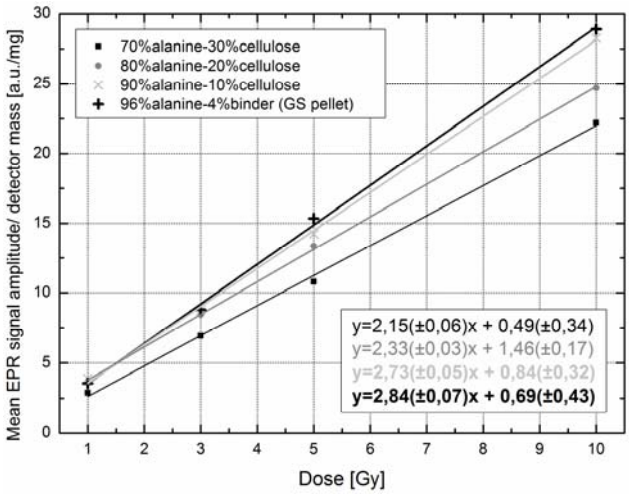

Fig. 3 – Preliminary calibration curves obtained for in-house manufactured detectors with different alanine-to-cellulose ratio compared with commercial Gamma Service pellets. For transparency, uncertainties (error bars) are not shown.

5. SUMMARY AND CONCLUSIONS

In this study we confirmed the applicability of the alanine detector as a potential element of the Quality Assurance system of patient and ion beam dosimetry in proton radiotherapy. The main advantages of alanine: linearity of dose response over the therapeutic range, lack of dependence of relative efficiency (with respect to Co-60 reference γ-rays) over the region of extended Bragg peak and ability to measure doses received by the patient in a cumulative fashion, make alanine a promising detector for QA purposes in clinical proton radiotherapy. We expect to be able to produce our own alanine detectors which would best suit our specific needs in terms of size and mechanical stability.

In suitable conditions (dark and dry storage) the radiation-induced signal in alanine is stable, thus the irradiated detector can serve as additional documentation of the patient's exposure over the therapy course. This signal can be measured repeatedly since the read-out procedure does not affect (or destroy) the signal. It is then possible to re-assess patient exposures at any time after completing the course of their radiotherapy, *e.g.* for verification, control or research purposes.

We are planning to use alanine in proton beam dosimetry and for patient dosimetry. Alanine detectors will be then irradiated in the proton beam prior to treating the patient and also in the part of beam directed at the target volume which is not modified by the individual collimator, as a form of *in vivo* dosimetry (the detector cannot be placed directly in the part of the beam which irradiates the target volume, as it would interfere with the planned dose distribution in the tumour volume). Most likely, the alanine detector will be placed inside the individual brass collimator and be read out following each radiotherapy session (fraction) to verify the dose received by the target volume, in cumulative fashion. Work on this stage of the project of applying the alanine detector for Quality Assurance in proton radiotherapy is under way [12].

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