Use of alanine for dosimetry intercomparisons among Italian radiotherapy centers

C. De Angelis*, V. De Coste, P. Fattibene, S. Onori, E. Petetti

Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy

Abstract

A pilot program of postal dosimetry intercomparison among 16 Italian Radiotherapy Centers was performed using the ISS Alanine/EPR dosimetry as a transfer system. Dosimeters were irradiated at 10 Gy with high-energy photon beams, both in reference condition in a water phantom and in an anthropomorphic phantom during the simulated treatment of rectum cancer. Intercomparison design along with alanine performances analyzing the different contributions to the combined uncertainty in dose assessment are reported. Main results of the pilot intercomparison, terminated in 2002, are also presented.

Keywords: Dosimetry intercomparison; Quality assurance in radiotherapy; Alanine dosimetry

1. Introduction

Clinical audits are generally considered of primary importance in improving quality in the radiotherapy process. They are accepted as a potential tool able to put in evidence problems in the complex step sequence involved in the patient treatment and to find out systematic errors in dose delivery. For instance, this was recognized and given emphasis by the European Commission (EC) in the Council Directive 97/43/EURATOM (MED-directive), where the Member States are required to implement clinical audits in accordance with national procedures. In the past, many dosimetry intercomparison programs, at national and international level, were promoted among Radiotherapy Centers (see for instance Horiot et al., 1986; Johansson et al., 1986; Wittkämper et al., 1987; Svensson et al., 1989; Hanson et al., 1991; Derreumaux et al., 1995). Recently, in 1998, an European Society for Therapeutic Radiology and Oncology (ESTRO) quality assurance network for radiotherapy (EQUAL) was set up for European countries (Ferreira et al., 2000). In Italy, the Istituto Superiore di Sanità (ISS, Italian National Institute of Health), in the framework of a national project, promoted and performed, during the years 2000–2002, a pilot program of dosimetry intercomparison among 16 Italian Radiotherapy Centers for high-energy photon beams. The ISS operated in collaboration with an experts’ committee, with participation of representatives of radiation oncologists, medical physicists and technicians, belonging to the same radiotherapy centers to be audited. As a consequence of the positive experience of the pilot project, the Italian Ministry of Health funded a new project with the aim to extend the dosimetry intercomparison to the other Italian radiotherapy centers. The goal of the Italian intercomparison is to verify, on a national base, the compliance of the dose stated by each radiotherapy center with the dose measured by ISS, acting as the reference center. Dosimeters are irradiated both in reference condition in a water phantom and in an...
anthropomorphic phantom during the simulated treat-
ment of rectum cancer (treatment condition). The
treatment modality is one of the peculiarities of the
italian intercomparison with respect to other similar
programs. Indeed, to the author knowledge, only a few
data are available in the literature concerning irradiation
in treatment conditions (Wittkämper et al., 1987; Kron
et al., 2002). The introduction of this kind of irradiation
modality is important to promote the participation of all
the various professionals involved in the radiotherapy
process, i.e. radiation oncologists, medical physicists and
technicians. This aspect has been considered relevant for
the success of the intercomparison itself and for the
development and implementation of the quality im-
provement programs in radiotherapy centers.

Another peculiarity of the Italian intercomparison
relates to the use of the alanine/EPR dosimetry system,
instead of the widespread TLD, for dose measurement.
This choice was taken on the basis of the positive alanine
characteristics such as tissue equivalence, dose rate and
energy independence, high stability of the response,
small dimension, non-destructive read out procedure,
robustness, etc.

In this work the alanine readout procedure, the
evaluation of uncertainty in dose assessment, as well as
the quality controls performed on the alanine/EPR
dosimetry operated by ISS are described. Also, main
results obtained in the pilot phase are presented.

2. Materials and methods

Each of the 16 centers participating to the pilot
program of intercomparison was asked to perform
irradiation both in reference and treatment conditions.
The alanine/EPR dosimetry operated by ISS was used as
a postal transfer system.

2.1. Reference condition irradiation

The absorbed dose to water in reference condition was
measured in a water phantom with the transfer
dosimeters placed at 10 cm in depth, 10 cm × 10 cm field
size of high-energy photons, 100 cm source surface
distance (SSD). In Fig. 1 a sketch of the phantom with
the set-up used for irradiation is reported. Each radio-
therapy center was asked to irradiate alanine dosimeters
with a photon beam of energy in the (6–18) MV range at
10 Gy dose. Three dosimeters had to be irradiated,
successively.

2.2. Treatment condition irradiation

Rectum cancer treatment with four opposed field
irradiation technique was chosen for the treatment
condition. A section of an anthropomorphic phantom
was used for the simulated treatment. Each radiotherapy
center had to irradiate at 10 Gy the dosimeter placed at
the isocenter using the same photon energy employed in
the reference condition irradiation. Centers were asked
to evaluate the monitor units necessary to give the
prescribed dose at the isocenter, performing the entire
treatment planning process (computerized tomography
(CT) scans, treatment planning system (TPS) dose
calculation, plan implementation, etc.) before dose
delivery.

The slice of the anthropomorphic phantom containing
the isocenter and the irradiation scheme are reported in
Fig. 2. The treatment was performed irradiating,
successively, two alanine dosimeters placed at the
isocenter, at 10 Gy dose level.

To evaluate relative dose distribution, also TLD,
positioned in five selected points inside the treatment
volume, chosen in low field gradient regions of clinical relevance, were used. In addition, a point outside, in correspondence of the bladder, was selected. These results are outside the scope of this paper and will not be included.

2.3. Alanine/EPR transfer dosimetry

Alanine pellets, 2 mm in length and 4.9 mm in diameter, were prepared at ISS using 95% of alanine and 5% of polyethylene by weight.

A Bruker–Elexsys spectrometer operating in the X band is used for EPR measurements. The EPR parameters are: 8 mW microwave power, 2.5 mT sweep field, 320 ms time constant, 1 mT modulation amplitude. A stack of five alanine pellets (in the following referred to as an alanine dosimeter) are used for each point of dose measurement. Each set of five pellets (i.e. one dosimeter) is inserted as a stack in a quartz tube for EPR measurement. To average out possible anisotropy of alanine dosimeter, the mean value of five repeated EPR measurements, obtained taking out and randomly repositioning the stack in the cavity, is taken for each dosimeter.

The ISS alanine dosimeters were calibrated in terms of dose to water in a 60Co gamma ray field at the Italian Primary Standard Dosimetry Laboratory (INMRI-ENEA). Calibration doses were given in the 6–14 Gy range with an uncertainty of 0.6% (1 standard deviation, SD, level). Four dosimeters were used for each calibration dose. Alanine response was linear in the calibration dose range with a maximum residual of 1%. Temperature correction factor was applied to the alanine EPR signal, while no correction factors were used for energy dependence (Sharpe et al., 1996) and fading (De Angelis et al., 2000). Sensitivity variations of the EPR spectrometer were compensated with an home made standard, consisting of a 100 Gy irradiated alanine dosimeter, sealed in a quartz tube and stored in the dark at laboratory conditions. The alanine standard is repeatedly measured during each measurement section.

2.4. Quality control on alanine/EPR dosimetry

Before starting and during the intercomparison, the reliability of the ISS alanine/EPR system was checked through periodic blind tests at INMRI-ENEA.

Many centers participating to the Italian intercomparison participated also to the ESTRO/EQUAL intercomparison. The simultaneous presence of clinical audit programs at national and international levels calls for a common traceability of the reference dosimetry systems operated by the different dosimetric laboratories. Then, as preliminary step, it was agreed on the utility to compare the TLD system operated by the Institut Gustave Roussy (IGR) with the alanine/EPR system operated by ISS. The aim was to show the equivalence, within the experimental uncertainty, of the dose measured by the two reference laboratories (IGR and ISS).

3. Results

3.1. Quality controls on alanine/EPR dosimetry

The comparison between the TLD system, operated by the ESTRO-EQUAL program and installed at the IGR (France), and the alanine/EPR system, operated by the Istituto Superiore di Sanità (Italy), was performed irradiating, in reference conditions, both dosimeter types with 60Co source and high energy photons produced by linear accelerator. The irrations were carried out at IGR and the Spedali Civili (SC), Brescia, Italy. 2Gy were delivered to TLDs and 10Gy to alanine dosimeters. The mean values of the measured dose to the stated dose for the different beam qualities are reported in the second and third columns of Table 1, for ISS alanine and ESTRO TLD, respectively (data are extensively reported elsewhere, Onori et al., 2003). Data reported in Table 1 show a strict agreement of the two dosimetry systems, within the combined uncertainty (2% for 60Co and 2.5% for megavoltage photon beams). The maximum difference between alanine and TLD doses was 1.3%. The value of the alanine to TLD dose ratio averaged over the various energies tested was 1.001 ± 0.008.

Moreover, the reliability and traceability of the alanine/EPR system has been assured by periodic blind tests at INMRI-ENEA with a 60Co source. For the years 2001 and 2002, six blind tests were performed. The mean value of the ratio of the absorbed dose to water measured by ISS and stated by INMRI-ENEA was 1.002 ± 0.007.

Table 1

<table>
<thead>
<tr>
<th>Beam quality</th>
<th>Alkaline dose</th>
<th>TLD dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stated dose</td>
<td>Stated dose</td>
<td></td>
</tr>
<tr>
<td>(10 Gy)</td>
<td>(2 Gy)</td>
<td>Mean value ± 1 SD (%)</td>
</tr>
<tr>
<td>60Co</td>
<td>1.002 ± 0.6</td>
<td>0.993 ± 0.7</td>
</tr>
<tr>
<td>6 MV</td>
<td>1.000 ± 0.3</td>
<td>0.994 ± 0.6</td>
</tr>
<tr>
<td>18 MV</td>
<td>0.985 ± 0.5</td>
<td>0.988 ± 0.4</td>
</tr>
<tr>
<td>20 MV</td>
<td>0.995 ± 0.4</td>
<td>1.004 ± 0.6</td>
</tr>
</tbody>
</table>
3.2. Intercomparison results

Results of the Italian intercomparison in terms of the alanine measured dose to center stated dose ratio, \( \frac{D_{\text{meas}}}{D_{\text{stated}}} \), are reported in Fig. 3. Fig. 3a and b show the results obtained in reference and in treatment conditions, respectively. Data are the mean values of 3 and 2 repeated irradiations, respectively. To directly compare the results among radiotherapy centers, correction factors were applied to \( D_{\text{stated}} \). They were evaluated taking into account differences among dosimetry protocols used by the centers for dose determination, as well as between physical quantities (air kerma or absorbed dose to water) used for the calibration of the center and alanine dosimetry systems. In Fig. 3a and b also the tolerance levels are shown. They were evaluated on the basis of the combined uncertainty in \( \frac{D_{\text{meas}}}{D_{\text{stated}}} \). The combined uncertainty was estimated considering the contributions to the uncertainty deriving from all the steps of the procedure chain applied in the intercomparison. The main contributions to uncertainty come from calibration of the center dosimetry system, alanine uncertainty, monitor units stability, CT scans, and TPS dose evaluation. The combined uncertainty was evaluated considering the alanine uncertainty and using the recent IAEA estimation of uncertainty in reference condition reported in the protocol 398 (IAEA 398, International Atomic Energy Agency, 2000) and data reported in the literature (Kutcher et al., 1994).

In Table 2 the detail of the different contributions to the alanine combined uncertainty is reported (1 SD). The values reported in rows 2, 3 and 4 were stated by INMRI-ENEA. The type A uncertainty in the alanine dose, determined from the calibration curve, is derived from the Eisenhart formula (Montgomery and Peck, 1982) for a test dose of 10 Gy. The 0.4% type B alanine uncertainty relates to the application of correction factors for compensating (1) temperature variations between irradiation at INMRI-ENEA for calibration and at the centers during audit, and (2) sensitivity variations of the EPR spectrometer.

In Table 3 an estimation of the specific components involved in the combined uncertainty of the \( \frac{D_{\text{meas}}}{D_{\text{stated}}} \) ratio is reported. The uncertainty contribution related to the alanine irradiation at the center is dominated by the stability of the monitor units. The component of dose evaluation comprises the additional steps related to the irradiation of the anthropomorphic phantom (mainly CT scans and TPS dose evaluation). Combined uncertainties of about 2.5% (1 SD) and 3% (1 SD) were estimated for the mentioned ratio in reference and treatment conditions, respectively. These figures were taken into account to determine the tolerance level for the \( \frac{D_{\text{meas}}}{D_{\text{stated}}} \) ratio. The tolerance level was defined as the range of values that the ratio would assume, at 95% probability level, repeating measurements. Therefore, tolerance levels of ±5% (2 SD) and ±6% (2 SD) were chosen for reference and

<table>
<thead>
<tr>
<th>Uncertainty component</th>
<th>A type (%)</th>
<th>B type (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary standard calibration, ( N_{Dw} )</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Long term stability of the secondary standard</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Calibration of alanine</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Calibration curve determination</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Alanine correction factors</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td><strong>Combined uncertainty</strong></td>
<td><strong>1.1</strong></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3. Results of the Italian intercomparison: (a) reference condition and (b) treatment condition. Bold lines are the mean values of the \( \frac{D_{\text{meas}}}{D_{\text{stated}}} \) ratio. Dotted lines represent the tolerance levels, ±5% and ±6% for reference and treatment conditions, respectively.
treatment conditions, respectively. Fig. 3a shows that, in reference conditions, the $D_{\text{meas}}/D_{\text{stated}}$ ratio was well within the tolerance level. The mean value of the $D_{\text{meas}}/D_{\text{stated}}$ ratio was 1.009 with a SD of 1.6%. The maximum deviation from unity was 2.9%.

As shown in Fig. 3b, also in the treatment condition all the centers were within the tolerance level of ±6%. The mean value of the $D_{\text{meas}}/D_{\text{stated}}$ ratio was 1.009±2.2% (1 SD) with a maximum deviation from unity of 4.1%. The increase in the dispersion of data from reference (1.6%) to treatment (2.2%) conditions, indicates that the treatment planning process introduces an additional uncertainty in dose delivery of about 1.5% with respect to the reference conditions.

4. Conclusions

The alanine/EPR dosimetry system operated by ISS has been proven suitable as a transfer system for postal dosimetry intercomparison in radiotherapy, complementing the widespread TLD system. Traceability to primary standards of absorbed dose to water and an high level of reliability in dose to water measurement were assured through periodic intercomparison with the Italian Primary Standard Dosimetry Laboratory and with a dose intercomparison with the TLD system operated by IGR in the framework of the ESTRO/EQUAL program.

The use of the ISS alanine/EPR system in the dosimetry intercomparison pilot project among 16 Italian radiotherapy centers proved alanine feasible for the extension of the intercomparison on a national scale. The results so far obtained, even if partial, indicate a good level of the Italian radiotherapy centers.

<table>
<thead>
<tr>
<th>Uncertainty component</th>
<th>Reference condition (%)</th>
<th>Treatment condition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine calibration</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Center dosimetry calibration</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Alanine irradiation at the center</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Dose evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined uncertainty</td>
<td><strong>2.5</strong></td>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>

**References**


