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The 4th international comparison on EPR dosimetry with tooth enamel Part 1: Report on the results

P. Fattibene
Istituto Superiore di Sanità, paola.fattibene@iss.it

A. Wieser
Helmholtz Zentrum Muenchen

E. Adolfsson
Linköping University

L. A. Benevides
Naval Dosimetry Center

M. Brai
University of Palermo

See next page for additional authors

Authors
P. Fattibene, A. Wieser, E. Adolfsson, L. A. Benevides, M. Brai, F. Callens, V. Chumak, B. Ciesielski, S. Della Monaca, K. Emerich, H. Gustafsson, Y. Hirai, M. Hoshi, A. Israelsson, A. Ivannikov, D. Ivanov, J. Kaminska, Wu Ke, E. Lund, M. Marrale, L. Martens, C. Miyazawa, N. Nakamura, W. Panzer, S. Pivovarov, R. A. Reyes, M. Rodzi, A. A. Romanyukha, A. Rukhin, S. Sholom, V. Skvortsov, V. Sepanenko, M. A. Tarpan, H. Thierens, S. Toyoda, F. Trompier, E. Verdi, and K. Zhumadilov

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P. Fattibene [a,*,1], A. Wieser [b,1], E. Adolfsson [c], L.A. Benevides [d], M. Brai [e], F. Callens [f], V. Chumak [g], B. Ciesielski [h], S. Della Monaca [a,i], K. Emerich [h,j], H. Gustafsson [c], Y. Hirai [k], M. Hoshi [l], A. Israelsson [c], A. Ivannikov [m], D. Ivanov [n], J. Kaminska [h], Wu Ke [o], E. Lund [c], M. Marrale [e], L. Martens [f], C. Miyazawa [p], N. Nakamura [k], W. Panzer [b], S. Pivovarov [q], R.A. Reyes [r], M. Rodzi [l], A.A. Romanyukha [d], A. Rukhin [q], S. Sholom [g,2], V. Skvortsov [m], V. Stepanenko [m], M.A. Tarpan [f], H. Thierens [f], S. Toyoda [s], F. Trompier [t], E. Verdi [b], K. Zhumadilov [l]

[a] Istituto Superiore di Sanità, Department of Technology and Health, Viale Regina Elena 299, I-00162 Rome, Italy
[b] Helmholtz Zentrum Muenchen, Neuherberg D-85764, Germany
[c] Linköping University, SE-58185 Linköping, Sweden
[d] Naval Dosimetry Center, Bethesda MD 20889-5600, USA
[e] University of Palermo, I-90128 Palermo, Italy
[f] Ghent University, B-9000 Gent, Belgium
[g] Research Center for Radiation Medicine AMS, 04050 Kiev, Ukraine
[h] Medical University of Gdansk, 80-211 Gdansk, Poland
[i] Regina Elena Institute, I-00144 Rome, Italy
[j] Department of Paediatric Dentistry, 80-208 Gdansk, Poland
[k] Radiation Effects Research Foundation, Minami-ku, Hiroshima 732-0815, Japan
[l] Hiroshima University, Minami-ku, Hiroshima 734-8553, Japan
[m] Medical Radiological Research Center, Obninsk, Kaluga region, Russia
[n] Institute of Metal Physics, Yekaterinburg 620041, Russia
[o] Beijing Institute of Radiation Medicine, Beijing 100850, China
[p] Department of Dentistry, Ohu Univesity, Japan
[q] Institute of Nuclear Physics, Almaty 050032, Kazakhstan
[r] Uniformed Services University of the Health Sciences, Bethesda, MD, USA
[s] Okayama University of Science, Okayama 700-0005, Japan
[t] Institut de Radioprotection et de Sûreté Nucléaire, F-92262 Fontenay-aux-Roses Cedex, France

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ABSTRACT

This paper presents the results of the 4th International Comparison of *in vitro* electron paramagnetic resonance dosimetry with tooth enamel, where the performance parameters of tooth enamel dosimetry methods were compared among sixteen laboratories from all over the world. The participating laboratories were asked to determine a calibration curve with a set of tooth enamel powder samples provided by the organizers. Nine molar teeth extracted following medical indication from German donors and collected between 1997 and 2007 were prepared and irradiated at the Helmholtz Zentrum München. Five out of six samples were irradiated at 0.1, 0.2, 0.5, 1.0 and 1.5 Gy air kerma; and one unirradiated sample was kept as control. The doses delivered to the individual samples were unknown to the participants, who were asked to measure each sample nine times, and to report the EPR signal response, the mass of aliquots measured, and the parameters of EPR signal acquisition and signal evaluation. Critical dose and detection limit were calculated by the organizers on the basis of the calibration-curve parameters obtained at every laboratory. For calibration curves obtained by measuring every calibration sample three times, the mean value of the detection limit was 205 mGy, ranging from 56 to 649 mGy. The

* Corresponding author. Tel.: +39 06 4990 2248.
E-mail address: paola.fattibene@iss.it (P. Fattibene).
[1] Equally contributing authors.
[2] Present address: Oklahoma State University, Stillwater, OK 74074, USA.

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participants were also invited to provide the signal response and the nominal dose of their current dose calibration curve (wherever available), the critical dose and detection limit of which were also calculated by the organizers.

1. Introduction

Dosimetry based on the electron paramagnetic resonance (EPR) measurement of radiation-induced radicals in tooth enamel is an established method for the retrospective assessment of dose. It is a method used for validating dosimetry in epidemiological studies (Degteva et al., 2005; Wieser et al., 2006a) and post-accident scenarios (Skvortsov et al., 2000). A significant number of laboratories around the world have set up this method by developing specific protocols of measurement. Since 1996 several international comparison programmes of EPR tooth dosimetry have been devised to assess the state of the art, and disseminate the expertise among laboratories (Chumak et al., 1996; Wieser et al., 2000, 2005, 2006b; Hoshi et al., 2007; Ivannikov et al., 2007). Regardless of their design, these inter-laboratory comparisons were all aimed at examining the capability of the participating laboratories to assess an unknown dose delivered to teeth.

In spite of the fact that EPR/tooth enamel dosimetry is a well established method, the procedures for the evaluation of measurement uncertainty and of the detection capability of the method have been neither harmonized nor standardized. The lack of a standard procedure makes it difficult to compare the results from different laboratories. This is typically the case with epidemiological studies where the very large amount of samples requires the contribution of several measuring laboratories.

The present inter-laboratory comparison was promoted under the EU project SOUL (SOUL, 2005) and aimed at proposing, and hopefully establishing, a common approach for the determination of the lowest detectable dose by the EPR/tooth enamel method. The comparisons between 1996 and 2006 were, therefore, different from this one where participants were not requested to asses an unknown dose.

The current international standards for determination of detection capabilities in chemical-metrology of the International Organization for Standards (ISO) and the International Union of Pure an Applied Chemistry (IUPAC) are harmonized with respect to the use of the concept of hypothesis testing on basis of type-I (α: false positive) and type-II (β: false negative) errors. Some differences exist in terminology and definitions (values of α and β) in the international standards to describe the detection capability of a method. Chemical-metrology uses the terms *critical level* and *detection limit* (Currie, 2004; IUPAC, 1995; ISO, 1997). For ionizing radiation measurements, ISO (1998) uses *decision threshold* and *detection limit*; sometimes the detection limit is also referred to as *minimum detectable (true) value* (IUPAC, 1995). In the analysis here the terminology *critical level* and *detection limit* and its definitions in the standards for chemical-metrology with $\alpha = \beta = 0.05$ was used (Currie, 2004).

A method for the evaluation of critical level and detection limit in EPR dosimetry with tooth enamel was suggested and tested in three laboratories, as described in Wieser et al. (2008). The aims of the present inter-laboratory comparison were i) to share and disseminate the methodology suggested in Wieser et al. (2008) among a large number of laboratories in order to find a common field of discussion, hopefully leading to the harmonization of the method; ii) to evaluate the applicability of this approach to a large number of laboratories.

The quantity of data (both results and details on measurement protocols) collected from the participants was large and their complete analysis will be done in several steps. This first paper will report the measurement results. As a preliminary analysis of the data, performance parameters were evaluated under the homoscedastic assumption. The calculation of the performance parameters under the heteroscedastic assumption (which applies better to EPR dosimetry with tooth enamel) requires the evaluation of an analytical model function of the variance in dependence on the absorbed dose (Wieser et al., 2008). This further evaluation, as well an analysis of the correlation of the performance parameters with specific features of the measurement procedures was not within the scope of this paper and it will be developed in a future analysis.

2. Materials and methods

2.1. Samples

Nine molar teeth (eight wisdom teeth and one second molar tooth) were collected from German people born between 1971 and 1989. The teeth were extracted following medical indication in 1997 and 2007. The samples were prepared according to the protocol of the Helmholtz Zentrum Muenchen (HMGU). Roots were removed mechanically and crowns were cut into halves. The pieces of crown were etched with a 0.1 M Titriplex(III) solution. Dentine was separated from enamel by a chemical treatment of 5 M NaOH in an ultrasonic bath at 60–70 °C over 15 h. The dentine remaining on the enamel chips was manually removed with a dental drill. The enamel was then ground and sieved to a grain size in the range of 0.1–0.6 mm and etched with acetic acid. After sample preparation, the absorbed dose in the nine samples was individually measured with EPR; no excess doses above natural background were found. The absorbed dose in the nine samples was on average 41 ± 27 mGy. The samples were pooled and then separated in six aliquots of 550 mg. Five aliquots were irradiated with doses of 0.1, 0.2, 0.5, 1.0 and 1.5 Gy; one aliquot was kept unirradiated. Samples were irradiated with a ^{60}Co radiotherapy source (Type Eldorado) inside a Plexiglas phantom box with 5-mm-thick walls on all sides with a dose rate of 0.05 Gy/min at the outer surface of the box. Doses were delivered in units of air kerma. Irradiation was performed at HMGU by staff members not participating in the intercomparison. The correspondence between samples and dose was unknown to both organizers and participants.

After irradiation, four sets of six aliquots of 120 mg were formed, consisting of five exposed and one unexposed aliquots. The sets of samples were labeled *A1-A6*, *B1-B6*, *C1-C6*, and *D1-D6*.

2.2. Description of the inter-laboratory comparison

2.2.1. Sample distribution

The sixteen participating laboratories were divided in four groups. Within each group the first participant received one set of six aliquots of tooth enamel powder. Each participant was given one month to complete the measurements and report the results, after which they had to ship the set of samples to the second participant of the same group, and so on. The samples were dispatched to the first of the four groups of participants on March 2009. The sequence of the participants was agreed upon, accounting for the availability declared by the participants themselves.

2.2.2. EPR measurements at participating laboratories

Each laboratory was asked to measure nine times 100 mg of each of the six aliquots (i.e. for a total of 54 measurements). EPR measurements had to be performed after emptying and refilling the sample tube. The participants used their own EPR spectrum acquisition parameters and signal intensity evaluation procedures. Each participant was requested to report the EPR signal response (amplitude or intensity) of the measurements.

The participants could optionally provide the EPR signal response and the nominal dose of the data points of the calibration curve currently used in their laboratories.

2.2.3. Collection and dissemination of results

Each participant was requested to send the results within one month after receiving the samples. The collection of the results was completed by July 2009. The received data were analyzed at HMGU and at the Istituto Superiore di Sanità (ISS), and the final analysis was disseminated in September 2009. Sixteen laboratories from twelve countries took part in the exercise.

2.3. Algorithm for the calculation of performance parameters

2.3.1. Definitions of terms

Detection limit (DL) and critical level (CL) refer to two different concepts. The detection limit "specifies the minimum (true) value of the measurand (here the EPR signal intensity) which can be detected with a given probability β of error (see below, description of Fig. 1) using the measuring process in question" (ISO, 1998). The detection limit is then related to the inherent detection capability of a method (IUPAC, 1995). In other words, the detection limit allows a decision to be made whether the method under question is suitable for a given purpose of the measurement.

The critical level allows the measured signal to be distinguished from the background noise (i.e.) it is related to the minimum significant estimated dose (IUPAC, 1995). According to ISO (1998) it "allows a decision to be made for each measurement with a given probability α of error as to whether the result of a measurement indicates the presence of the physical effect quantified by the measurement". In other words, if the result of a measurement is higher than the critical level, then the measurement is detecting a physical effect, with a probability α of being false positive.

Fig. 1 gives a picture of these definitions in the heteroscedastic case (i.e. where the standard deviations of exposed and unexposed samples are different). As we said before, the concepts of critical level and detection limit are based on the principles of statistical hypothesis testing and on the probabilities of false positives α and false negatives β. In their simplest form (the so-called single concentration design), the critical level, I_{CL}, and the detection limit, I_{DL}, of EPR signal intensity are calculated by equations (1) and (2) from the mean of measurements of unexposed samples (b_0) and the estimated standard deviation of n EPR measurements of unexposed samples, $\hat{\sigma}_0$, and samples exposed to a dose D_{DL}. $\hat{\sigma}_{DL}$, respectively.

$$I_{CL} = b_0 + t_{(1-\alpha,n-2)}\hat{\sigma}_0 \quad (1)$$

$$I_{DL} = I_{CL} + t_{(1-\beta,n-2)}\hat{\sigma}_{DL} \quad (2)$$

The estimated standard deviation must be multiplied by the Student's critical value $t_{(1-[\alpha \text{ or } \beta],n-2)}$, the (1-[$\alpha$ or β]) percentage point of Student's t distribution with the single-sided confidence interval chosen according to the desired confidence level (1-[α or β]) and number of samples n. With the single concentration design the signal-to-dose response curve given by equation (3) must be known from other measurements in order to evaluate the critical level of dose (D_{CL}) and the detection limit of dose (D_{DL}) corresponding to the critical level and detection limit of signal intensity, respectively. Dose and signal intensity related to critical levels and detection limits can instead be assessed simultaneously with the so-called calibration design. In that case, the calculation must be based on the signal-to-dose response curve with prediction intervals (Fig. 2). In this paper the calibration design was implemented assuming that the distribution of EPR signal intensity at given absorbed dose can be taken as Normal with constant standard

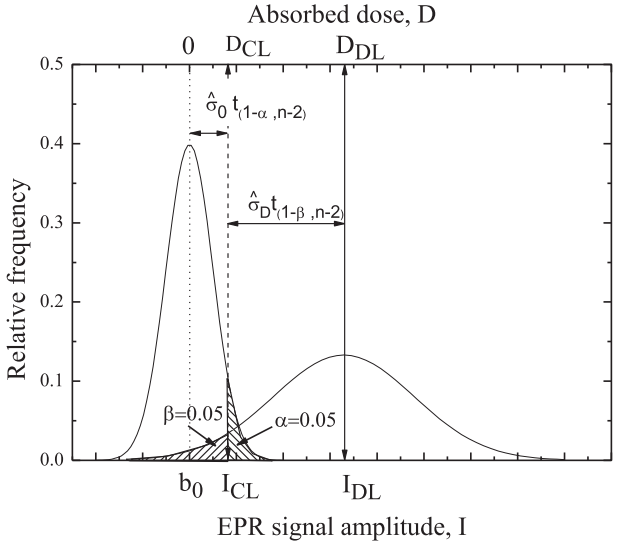

Fig. 1. Graphical representation of the single concentration design based performance parameters. The two curves are the relative frequency of the EPR signal amplitude for non irradiated samples (curve centered at the intercept b_0) and for samples irradiated at the detection limit (curve centered at I_{DL}). The top horizontal axis shows the dose related to the critical level and detection level of amplitude. Meaning of other symbols is given in the text.

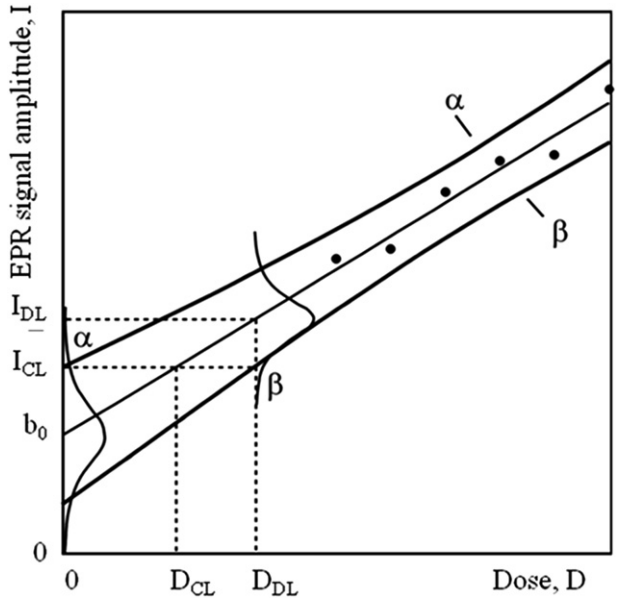

Fig. 2. Graphical representation of the calibration design based performance parameters as calculated in this work. Shown is the linear regression line of the measurements (full circles) together with upper and lower 90% prediction levels as calculated with standard methods. The width of the prediction band ($I_{CL} - b_0$) for the predicted EPR signal amplitude of unexposed samples (b_0) converted to dose units is equivalent to the critical level of dose (D_{CL}). Meaning of other symbols is given in the text.

deviation being independent on absorbed dose (homoscedastic approach). The linear signal-to-dose response curve was hence determined by unweighted fitting. The scope of this first part of the work was to set the basis for future analysis that will include dose-dependent variance modeling, and hence weighted fit of the dose response curve, which is required for the evaluation of critical level and detection limit with the heteroscedastic approach.

It should be pointed out that in practice the so-called 'non exposed' tooth enamel samples -i.e., samples which have not been irradiated in the laboratory- are actually never free of dose because of the unavoidable natural background radiation. Therefore, the terms critical dose and detection limit in fact mean critical dose and detection limit above background dose.

2.3.2. Calculation of the calibration design based performance parameters

In this study, the linear signal-to-dose response curve was determined by unweighted fitting and described by equation (3),

$$I = b_0 + b_1 \mathrm{D} \tag{3}$$

where I is the EPR signal intensity, D is the applied dose, b_0 is the intercept and b_1 the slope. For a tolerance level of $\alpha = \beta = 0.05$ for false positive and negative errors the critical levels of EPR signal intensity, I_{CL}, of dose, D_{CL}, and the detection limit, D_{DL}, can be evaluated in the calibration design from the 90% prediction bands of a linear least-squares fit of the EPR signal-to-dose response curve as illustrated in Fig. 2. Under these conditions, the critical level of EPR signal intensity, I_{CL}, and of dose, D_{CL}, are given by equations (4) and (5), respectively (equivalent to Zorn et al., 1997).

$$I_{CL} = b_0 + t_{(0.95,n-2)} s \left[1 + \frac{1}{n} + \frac{D_M^2}{SSD}\right]^{1/2} \tag{4}$$

$$D_{CL} = \frac{(I_{CL} - b_0)}{b_1} \tag{5}$$

where t is the critical value of the Student's t distribution for 95% single-sided confidence intervals, n the number of signal intensity-applied dose data pairs (I_i, D_i), D_M is the mean of all D_i and SSD is the square sum of dose variation given by equation (6). The residual standard deviation s is defined by equation (7), where I_i is the EPR signal intensity of the calibration point at dose D_i and I is the EPR signal intensity derived from the response curve of Eq. (3) for an applied dose D_i. All D_i within the same dose group are of identical value.

$$SSD = \sum (D_i - D_M)^2 \tag{6}$$

$$s = \sqrt{\frac{\sum (I_i - I)^2}{n-2}} \tag{7}$$

The detection limit, D_{DL}, is determined by equation (8).

$$D_{DL} = D_{CL} + \frac{t_{(0.95,n-2)} s}{b_1} \left[1 + \frac{1}{n} + \frac{(D_{DL} - D_M)^2}{SSD}\right]^{1/2} \tag{8}$$

Since D_{DL} also appears in the right term of the equation, Eq. (8) must be solved iteratively.

In the homoscedastic approach the standard uncertainties of the signal intensity from non exposed and exposed samples are assumed to be equal ($\sigma_0 = \sigma_{DL}$). Under this circumstances and the precondition of $\alpha = \beta$, it follows from equations (1), (2) and (3) that the detection limit of dose is twice the critical level ($D_{DL} = 2D_{CL}$). By evaluation of D_{DL} and D_{CL} in the calibration design the D_{DL}/D_{CL} ratio is approaching 2 only under special conditions as, e.g., with increasing number n of calibration data points ($1/n \to 0$, $D_M^2/SSD \to 0$) and with the detection limit approaching the mean applied dose of the dose response curve ($D_{DL} - D_M \to 0$) as can be seen from the comparison of Eq. (4)–(6) and (8). In the more common case of a limited number of data and a dose detection limit not equal to the mean dose of the dose response curve, the D_{DL}/D_{CL} ratio will be slightly lower than 2, as in Fig. 2. This demonstrates that with the precondition of constant variance the detection limit will be never larger than double of the critical dose level independent on the design of the calibration curve.

In this study critical level and detection limit of dose were evaluated from signal-to-dose response curves constructed by pooling the measurements in three ways: a) the 54 measurements as such (no pooling); b) for each calibration dose, the nine measurements were pooled in three groups of three measurements in the order as reported by the participants; c) for each calibration dose, the nine measurements were pooled together. These three averaging methods will be indicated with subscripts (1), (3) and (9), respectively. For all

Table 1
Calculated performance parameters of the calibration curves calculated by the participants using the standard set of samples provided by the organizers. Dose intercept, b_0, is reported in column 2. Detection limit and D_{DL}/D_{CL} ratios for the three designs of signal-to-dose response curves are reported in columns 3–8.

ID	b_0 (mGy)	$D_{DL(1)}$ (mGy)	$D_{DL(3)}$ (mGy)	$D_{DL(9)}$ (mGy)	$D_{DL}/D_{CL(1)}$	$D_{DL}/D_{CL(3)}$	$D_{DL}/D_{CL(9)}$
1	60	219	113	105	1.994	1.990	1.977
2	40	64	56	60	1.998	1.995	1.987
3	−90	124	103	64	1.996	1.991	1.986
4	116	151	78	57	1.996	1.993	1.987
5	28	151	158	235	1.996	1.987	1.955
6	312	691	649	550	1.990	1.974	1.933
7	350	292	224	206	1.993	1.983	1.960
8	117	187	127	19	1.995	1.989	1.996
9	22	219	182	56	1.993	1.983	1.987
10	636	353	286	346	1.992	1.980	1.942
11	51	141	98	112	1.996	1.992	1.976
12	58	145	95	125	1.996	1.992	1.973
13	60	134	96	36	1.996	1.992	1.992
14	299	379	312	138	1.992	1.979	1.971
15	49	137	93	65	1.996	1.992	1.985
16	984	829	616	644	1.993	1.974	1.935
Mean value		263	205	176	1.994	1.987	1.971
σ		213	182	186	0.002	0.007	0.020

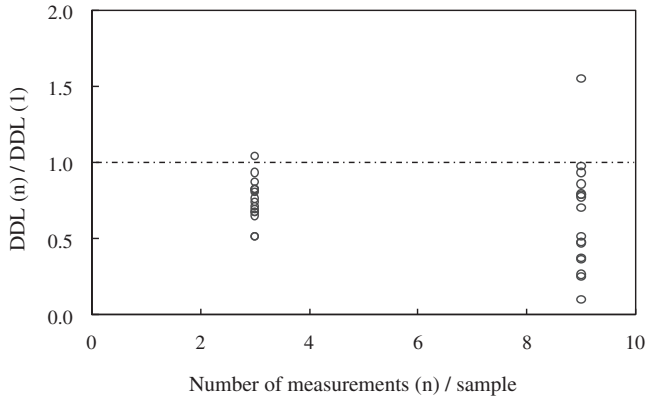

Fig. 3. Ratio of detection limit of dose with n measurements of a sample, $D_{DL}(n)$, to the detection limit of a single measurement of a sample, $D_{DL}(1)$, for all participants. The dashed line indicates the border line outside of which increase and decrease of ratio of detection limits occur with increasing measurement number.

Table 2
Parameters of the calibration curves provided by the participants (columns 2–5), calculated detection limits (columns 6–8) and D_{DL}/D_{CL} ratios (columns 9–11) for the three designs of signal-to-dose response curves.

ID	Measurements per dose	No. of doses	b_0 (mGy)	D_M (mGy)	$D_{DL(1)}$ (mGy)	$D_{DL(3)}$ (mGy)	$D_{DL(all)}$ (mGy)	$D_{DL}/D_{CL(1)}$	$D_{DL}/D_{CL(3)}$	$D_{DL}/D_{CL(all)}$
2	9	5	60	370	108	94	88	1.995	1.986	1.968
4	15	6	172	551	221	190	161	1.996	1.992	1.968
5	4 (0 Gy: 12)	6	−3	350			117			1.961
6	15	6	265	553	553	651	422	193	1.995	1.985
7	6	10	312	1150	414	319	215	1.996	1.992	1.989
8	8 (1 Gy: 10)	5	−1	718	136	91	9	1.991	1.986	1.997
9	3(0 Gy: 9)	6	74	350	208	194	197	1.988	1.968	1.943
11	1	5	182	400	170			1.935		
13	15	6	21	550	161	134	66	1.997	1.993	1.985
14	5 (0 Gy: 9)	7	334	538	575	569	159	1.986	1.963	1.964
Mean value					294	251	134	1.987	1.983	1.971
σ					202	172	69	0.020	0.011	0.017

applied doses the course of results in the order as reported by the participants did not show any obvious systematic trend therefore the results were not further randomized before forming the groups of three from the nine measurements. The above described pooling of results corresponds to the expected performance of laboratories if they routinely report dose results from a) single, b) mean of three, and c) mean of nine measurements of a sample.

Moreover the critical level and the detection limit of dose were derived also for the participants' calibration curves, in order to compare the effect of different calibration curve designs on the performance parameters of a certain laboratory.

The calculation algorithm was also distributed among the participants so that they could perform calculations individually.

3. Results and discussion

3.1. Performance parameters of the calibration curves determined with the comparison samples

Table 1 reports the dose detection limits calculated for the three different design response curves (ungrouped, mean of three and mean of nine measurements per dose, indicated by subscripts (1), (3) and (9), respectively)) determined with the comparison samples, together with the mean value and the associated standard deviation of the participant's detection limits. For two laboratories (IDs 6 and 16) the dose detection limit was outside the interval of two standard deviations. By excluding such outliers, the mean value of the dose detection limit was 193 ± 91 mGy for the ungrouped measurements, 144 ± 79 mGy for the measurements pooled in three groups of three, and 116 ± 91 mGy for the measurements pooled in one group of nine.

On average an evident decrease in the detection limit with increasing grouping was observed (Fig. 3). The mean reduction of the dose detection limit was (24 ± 14) % and (36 ± 36) % for groupings of three and nine measurements, respectively. There was a huge variability in the detection limit from different laboratories with increasing number of measurement ranging from a decrease of 48% and 90% to an increase of 5% and 56% for groupings of three and nine measurements, respectively. Reasons for this huge variability were not investigated here in the first analysis of results.

The ratio of dose detection limit to dose critical level (D_{DL}/D_{CL}) calculated for the three differently calibration curve designs derived with the comparison samples are reported in the last three columns of Table 1. The mean ratios were 1.994 ± 0.002, 1.987 ± 0.007 and 1.971 ± 0.020 with the response curves for ungrouped, mean of three and mean of nine measurements, respectively. For all participants and all three designs of response curves the D_{DL}/D_{CL} ratios were on average not more than about 1.5% lower than 2. In the worst cases (IDs 6 and 16) when D_{DL} was close to the mean applied dose of 550 mGy of the signal-to-dose response curve and grouping of all nine measurements ($n = 6$), the D_{DL}/D_{CL} ratios were just about 3% lower than 2.

As an approximate and practical rule, assuming the designs of response curves used here and the homoscedastic case, the detection limit can be calculated from the critical level derived from the calibration curve design by multiplication with a factor of 2 within the above-mentioned uncertainty.

3.2. Performance parameters of the calibration curves currently in use at the participants' laboratories

Ten of the sixteen participants provided data of their signal-to-dose calibration curve for analysis. Table 2 reports the number of doses, the number of measurements per sample, the mean applied dose (D_M) and the dose intercept (b_0) of the calculated dose response linear fit. The mean applied dose of the calibration curves varied between 350 and 1150 mGy and the dose intercept varied between −3 and 334 mGy. The detection limits calculated from the calibration curves provided by the ten participants are reported in Table 2. The mean value of the detection limit was 294 ± 202 mGy for the ungrouped measurements, 251 ± 172 mGy for the mean of three measurements per sample, and 134 ± 69 mGy for the mean of all measurements per sample. The ratio of dose detection limit to

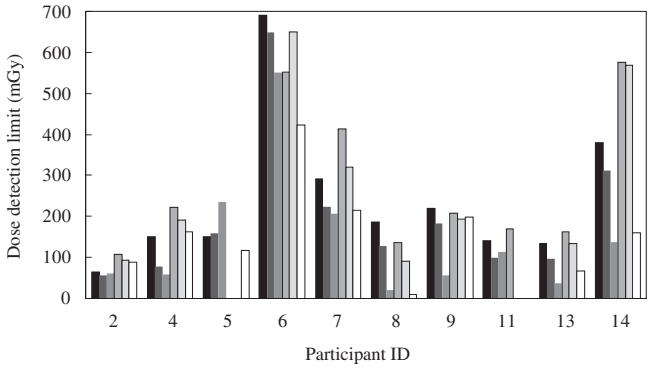

Fig. 4. Comparison of detection limits derived from measurements of the comparison samples and of participants own calibration samples for the ten participants who provided results of both measurements. From the darkest to the lightest gray columns: D_{DL} for single, mean of three and mean of nine measurements per dose for the comparison sample calibration curve and D_{DL} for single, mean of three and mean of all measurements per dose for the participant calibration curves. In measurements of the own calibration samples participant with ID5 provided only mean results of measurements per applied dose and ID11 performed only a single measurement per applied dose.

dose critical level (D_{DL}/D_{CL}) calculated for the three differently constructed response curves derived from the data of the participants calibration curves are also reported in Table 2. The mean ratios were 1.987 ± 0.020, 1.983 ± 0.011 and 1.971 ± 0.017 with the response curves for ungrouped, mean of three and mean of all measurements per sample, respectively. For all the calibration curves of the participants and all three kinds of measurement averaging, the D_{DL}/D_{CL} ratios were on average less than 1%, and in the worst case less than 3%, lower than 2. This confirms also for the participants' calibration curves that, in the homoscedastic approach, the detection limit can be calculated from the critical level by multiplication with a factor of 2 within the above-mentioned uncertainty.

For the ten laboratories who provided data of their own calibration curve the detection limits of dose derived from the measurements of the comparison samples, and of the participants' calibration curves are compared in Fig. 4. The mean value of the ratio of detection limits derived from the comparison samples and participants' calibration curves was 0.89 ± 0.28, 0.79 ± 0.31 and 1.01 ± 0.67 with the calibration curves for ungrouped, mean of three and mean of all measurements per sample, respectively. Two conclusions can be derived from these figures: a) the mean values of the ratio of detection limits were reasonably close to 1, showing an agreement between the estimated detection limits with both methods; b) the width of the distributions significantly increased with the averaged number of measurements. The increase was a factor of about three between averaging over all available measurements per sample and ungrouped measurements.

4. Conclusions

The goal of the present work was to start a process of sharing and spreading of a method for the evaluation of the detection limit in EPR/tooth enamel dosimetry, in order to have a common ground of discussion hopefully leading to the harmonization of the method. The methodology suggested in Wieser et al. (2008) was tested in sixteen laboratories. As a first approximation, variance of EPR measurements was assumed to be constant and independent of dose. The methodology provided reasonable results in all labs with an evident decrease in the detection limit with the increasing averaging of measurements per sample. For calibration curves obtained by measuring every calibration sample three times, the mean value of the detection limit was 205 mGy, ranging from 56 to 649 mGy. The detection limits evaluated in this paper apply to the specific calibration curve design and measurement conditions used. The reported detection limits can be considered as prediction for future measurements if they will be done using the same measurement parameters and grouping of results, the same kind of enamel sample preparation and the same dose response calibration curve. Any different feature of the measurement may lead to a different detection limit. In this analysis for ten participants detection limits were compared that were derived from differently designed calibration curves, one with the samples from this intercomparison and another with their own calibration samples. The mean ratio of detection limits derived from the comparison samples and participants' calibration curves was reasonably close to 1, showing an agreement between the estimated detection limits with both methods. This demonstrates that the applied methodology for assessing detection limits has the potential to evaluate the performance of a measurement system and is not predominatly influence by the design of the calibration curve.

In the homoscedastic approach the detection limit can be calculated from the critical level derived from the calibration curve design by multiplication with a factor of 2 with an uncertainty of less than about 3%.

Further studies will include: 1) the calculation of the critical value and the detection limit in the same participating laboratories, considering the dependence of variance on dose; 2) the correlation of specific features of the measurement protocol (EPR acquisition parameters, type of instrumentation, signal evaluation method) with the level of critical value and detection limit.

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