Original paper

Output factor measurement in high dose-per-pulse IORT electron beams

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ABSTRACT

Purpose: To assess the capability of different types of detectors to measure relative output factors (OF) at high dose per pulse by comparison with alanine dosimeters, which are independent of dose rate.
Methods: Measurements were made in 9 MeV and 7 MeV electron beams produced by a Novac7 accelerator for intraoperative radiotherapy. Applicators with diameter of 10-7-6-5 and 4 cm were used. The dose per pulse varied from about 30 mGy, for the 10 cm reference applicator, to about 70 mGy, for the 4 cm applicator. Five types of plane-parallel ionization chambers (PTW Advanced Markus, Markus and Roos, IBA PPC40 and PPC05), two types of silicon diodes (PTW 60017 and IBA EFD[3G]) and a PTW 60019 microDiamond were considered. For the ionization chambers, correction factors for ion recombination effects were determined for each applicator using a modified two-voltage-analysis method that includes the free-electron component.
Results: Reference OF values were determined by alanine dosimeters with a standard combined uncertainty of 0.8%. Deviations from the reference OFs were generally within 1.5% for all the detectors, hence within the 95% confidence interval of alanine measurements. Larger deviations of up to about 2% obtained in a few cases are consistent with a 0.7% long-term reproducibility of OF measurements.
Conclusions: Comparison with alanine measurements demonstrated that all the detectors considered in this work can be used to measure OFs in high dose-per-pulse electron beams with an accuracy better than 2%, provided that appropriate corrections for ion recombination effects are applied when using ionization chambers.

1. Introduction

Intraoperative radiotherapy (IORT) is a localized form of radiation therapy where a single high dose of radiation is delivered directly to the tumour bed during surgery, immediately after the resection [1–4]. The procedure adds no more than an hour to the total length of surgery, but the IORT treatment itself requires only a few minutes. A major advance in IORT came in the late 1990s with the introduction of mobile linear accelerators, such as the Mobetron® 1000 (IntraOp Medical, Inc. Santa Clara, CA) [5,6] and the Novac7 (Hitesys SpA, Aprilia, Italy) [7–9], specifically designed to operate directly in a conventional operating room. The Mobetron® 1000 consisted of an accelerator mounted on a motor driven gantry providing electron beams of 4, 6, 9 and 12 MeV with dose rate in the range 2.5–10 Gy min^{-1} at a source distance of 50 cm with an applicator of 10 cm diameter. The Novac7 consisted of a radiating unit and a control console. The accelerator operated at four nominal electron energies (3, 5, 7, 9 MeV) with a pulse repetition frequency of 5 Hz and a nominal dose rate in the range 9–21 Gy min^{-1}.

Later on, a new version of Novac7 (NRT, now merged with SIT, Vicenza, Italy) was introduced, operating at energies of 4, 6, 8, 10 MeV, 9 Hz pulse repetition frequency and dose rate in the range 6–39 Gy min^{-1} [10]. The experience accumulated over the years led to the realization of new models, such as the Novac11 (SIT, Vicenza, Italy), operating at the same energies and dose rates of the Novac7 [11,12], the Liac® 12 MeV (SIT, Vicenza, Italy) [12] and the Mobetron® 2000 (IntraOp Medical, Inc. Santa Clara, CA) [13]. The Liac® 12 MeV is a newly designed linac for IORT providing four clinical energy points: 6, 8, 10 and 12 MeV. The pulse repetition frequency can be varied from 1 to 60 Hz producing a dose rate in the range 3–40 Gy min^{-1}. The Mobetron® 2000 is lighter than the previous model, and generates electron beams with nominal energies of 6, 9, and 12 MeV at dose rates up to approximately 10 Gy min^{-1}.

Mobetron accelerators produce dose per pulse up to about 6 mGy and beam dosimetry can be performed following radiotherapy dosimetry protocols such as the IAEA TRS-398 and the AAPM TG-51 [14,15]. However, the high dose per pulse generated by the Novac7 and

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later models (up to about 100 mGy per pulse) poses specific dosimetric issues that have indeed received much attention over the last two decades. In particular, due to the high density of electric charge produced per radiation pulse, ionization chambers typically used in external beam radiotherapy dosimetry can't be employed for the calibration of IORT electron beams in terms of dose per monitor unit. In fact, the correction factor for ion recombination, k_s, is largely overestimated [16–18] when it is determined using correction methods proposed by currently available international dosimetry protocols [14,15]. Inaccuracies in the determination of k_s factors are produced by the free-electron fraction, p, which is not considered in the charge collection efficiency model of current protocols but has a significant impact in the determination of k_s in high dose-per-pulse beams [19,20]. In fact a fraction of the electrons produced by the radiation pulse in the air cavity does not attach to oxygen molecules and reaches the collecting electrode of the chamber. Then the excess in the positive ion concentration results in a reduction in ion recombination, i.e. an increase in collection efficiency.

As a consequence, the use of dose-rate-independent dosimeters instead of plane-parallel ionization chambers has been recommended for reference and relative dosimetry [21,22]. At present, the use of the Fricke absolute dosimetric system (chemical dosimeter based on a solution of ferrous sulphate) is suggested for the measurement of accelerator outputs in reference and non-reference conditions [4,17,18,21,23]. Alternative dosimetric systems with sensitivity independent from the dose rate, are alanine dosimetry [21,24,25] and gafchromic films [16,18,21,26–28].

Preliminary work on the saturation loss at high dose-per-pulse values was conducted in 2000 by Piermattei and co-workers [16]. The authors assessed the response of three plane-parallel ionization chambers (Markus type 23343, NACP-02 and Roos type 34001) using a Novac7 electron beam of 7 MeV nominal energy providing values of dose per pulse in the range 30–60 mGy. Radiochromic MD-55-2 films were selected as reference dosimeters for the Novac7 electron beam calibration. The authors found that the correction factor for ion recombination is overestimated (up to 20%) when it is determined using the two-voltage-analysis (TVA) method proposed by conventional international protocols. Over the last two decades, different approaches were suggested for the determination of the correction factor for ion recombination. In 1996, Boag et al. [20] proposed three improved models of the charge collection process in small ionization chambers exposed to pulsed radiation. All three models allow for the presence of a free-electron component in the charge transfer. In 2005 Di Martino et al. [18] proposed a new expression for k_s as a function of dose per pulse, derived from the general equation for collection efficiency based on the first model by Boag et al. 1996. Their approach, requiring an initial independent determination of the dose per pulse of the IORT beams, was validated by comparing the absorbed doses to water measured with plane-parallel ionization chambers (Roos and Markus) to that measured using radiochromic films and chemical Fricke dosimeters. In another paper, Laitano et al. [17] proposed another approach based on Boag's improved models. The authors determined k_s values for different ionization chambers avoiding chamber calibration against any dose-per-pulse-independent dosimeter. In their study the free-electron fraction was calculated as a function of chamber characteristics and experimental conditions.

Despite there being a vast amount of literature on the problem of ion recombination under IORT beams, on-line dosimetry in high dose-per-pulse beams is challenging and there is still no general consensus on the best measurement approach. As a consequence, over the last years a number of authors investigated the use of different detectors for IORT dosimetry, including output factor (OF) measurements.

Among available solid-state dosimeters silicon diode is commonly considered a suitable detector for relative dose measurements in IORT electron beams thanks to its small sensitive volume, high sensitivity and high spatial resolution [29,30]. However, a dependence of response on

dose rate, beam energy, and radiation incidence angle has been reported in literature for some types of silicon diode [31,32]. In recent years, a novel dosimeter based on a synthetic single crystal diamond was introduced in the market by PTW, Freiburg (microDiamond type 60019). Such dosimeter proved to be suitable for accurate dosimetry under IORT electron beams with dose per pulse up to 100 mGy [30].

The aim of this study was to investigate the capability of various types of plane-parallel ionization chambers (Advanced Markus, Markus, Roos, PPC40 and PPC05), two types of silicon diodes (PTW diode E and IBA EFD^{3G}), and the PTW microDiamond to correctly measure OFs under IORT electron beams with dose per pulse above 30 mGy. Reference OF values were obtained using alanine dosimeters, whose response is independent of dose rate and electron beam energy [33,34]. Of note, at the time of writing there are no literature studies on use of the two silicon diodes, Roos and PPC40 ionization chambers for the measurement of OFs at high dose per pulse.

2. Materials and methods

Output factors for clinical applicators were measured for 9 MeV and 7 MeV electron beams produced by a Novac7 mobile accelerator for IORT treatments. The dose per pulse was about 30 mGy with a dose rate of about 10 Gy min^{-1} in reference conditions and varied by up to a factor 2.5 for the clinical applicators. Different types of plane-parallel ionization chambers and solid-state detectors were used to measure OFs and results were compared with those obtained by means of alanine/EPR dosimetry.

2.1. Electron beams

Electron beams were produced by the Novac7 accelerator installed at the Papa Giovanni XXIII hospital in Bergamo (Italy). The accelerator is composed of a controlling console positioned near the operating room, and a motorized mobile unit consisting of a basement (motors and cooling system), an articulated arm with the modulator and a radiating head that contains the accelerating structure and the monitor-chamber system. The Novac7 does not use any scattering foil for beam broadening that is obtained by means of a hard-docking collimation system consisting of a set of polymethylmethacrylate (PMMA) cylindrical applicators that can be directly attached to the radiation head. The PMMA applicators have 5 mm wall thickness, internal diameter ranging from 3 cm to 10 cm and flat or bevelled end. The length of the applicators determines the treatment distance, which is 100 cm for the applicator with diameter of 10 cm and 80 cm for applicators with smaller diameters. The accelerator operates at four nominal electron energies (3, 5, 7 and 9 MeV) with a pulse repetition frequency of 5 Hz, a pulse duration of 4 μs and values of dose per pulse allowing to achieve dose rates in the range 10–25 Gy min^{-1} depending on beam energy and applicator size. Measurements of this work refer to 7 MeV and 9 MeV nominal energies and flat-ended applicators with diameters of 4, 5, 6, 7 and 10 cm.

For the dosimetric characterization of the beams percentage depth dose curves (PDD) and transversal beam profiles were measured in a water phantom by means of a PTW diode E type 60017. The dose per pulse at the depth of maximum dose was determined using alanine dosimeters.

2.2. Output factor determination

For a given electron beam nominal energy, OFs are defined as the absorbed dose to water at the depth of maximum dose for the set of different applicator diameters and treatment distances to the corresponding value under reference conditions. The reference conditions for the Novac7 beams were established using the largest available applicator, i.e. reference field size 10 cm in diameter and source to surface distance 100 cm [14,15,22].

Table 1

Characteristics of plane-parallel ionization chambers and solid-state detectors tested in this work for output factor measurement in high dose-per-pulse electron beams. For the ionization chambers V_1 represents the normal operating polarizing voltage, and V_2 the lowest polarizing voltage used for determining the ion recombination correction factor.

Plane-parallel ionization chambers				
Type	Air cavity diameter	Electrode spacing	Reference point	Polarizing voltage V_1; V_2
PTW 34045 (Adv.Markus)	5 mm	1 mm	1.3 mm below the protection cap surface	400 V; 100 V
PTW 34001 (Roos)	15 mm	2 mm	1.12 mm below the outer surface	400 V; 100 V
PTW 23341 (Markus)	5.3 mm	2 mm	1.3 mm below the protection cap surface	400 V; 100 V
IBA PPC05	10 mm	0.6 mm	1 mm below the outer surface	300 V; 100 V
IBA PPC40	16 mm	2 mm	1 mm below the outer surface	300 V; 100 V

Solid-state detectors				
Type	Sensitive volume diameter	Sensitive volume thickness	Reference point	Sensitive material
IBA EFD^{3G} (p-type unshielded diode)	2 mm	500 μm	0.58 mm from the detector surface	Silicon
PTW 60017 (p-type unshielded diode)	1.1 mm	30 μm	0.6 mm from detector tip	Silicon
PTW 60019 (microDiamond)	2.2 mm	1 μm	1 mm from detector tip	Diamond

OF measurements were carried out by means of a set of commercially available detectors widely used for electron beam dosimetry and results were compared to the reference OF values obtained with alanine dosimeters. Specifically we tested five types of plane-parallel ionization chambers (PTW Advanced Markus type 34045 (hereinafter Adv.Markus), Markus type 23341 and Roos type 34001, IBA type PPC40 and type PPC05), two types of electron silicon diodes (PTW diode E type 60017 and IBA EFD^{3G}), and a diamond detector (PTW microDiamond type 60019). A summary of the detector characteristics and measurements parameters are reported in Table 1. For the ionization chambers (IC), the polarizing voltage, V_1, was set to the maximum value allowed in the chamber datasheet (for PTW ICs) or to the value recommended by the manufacturer (for IBA ICs). To exclude the presence of spurious effects due to the high electric field in the air cavity, preliminary tests were performed to verify that the selected polarizing voltage was in the linearity range of the reciprocal of ionization signal, $1/M$, versus the reciprocal of applied voltage, $1/V$.

All the detectors were positioned with their reference point, as specified in the manufacturer's datasheet (see Table 1), at the depth of maximum dose in a PTW-MP3-XS water phantom, equipped with a 3D scanning system (detector position accuracy ± 0.1 mm). Detector signals were acquired using a PTW Unidos Webline electrometer.

For the solid-state detectors, including alanine, the OF was approximated by the ratio of detector signals obtained under non-reference and reference conditions for the same number of monitor units. For the ionization chambers possible variations of polarity and ion recombination effects with the beam size were accounted for and for a given beam quality Q and applicator diameter d, the OF was obtained as:

$$\text{OF}_{Q,d} = \frac{[M(z_{max,d})]_Q}{[M(z_{max,d=10cm})]_Q} \frac{[s_{w,air}(z_{max,d})]_Q}{[s_{w,air}(z_{max,d=10cm})]_Q} \frac{[k_s]_{Q,d}}{[k_s]_{Q,d=10cm}} \frac{[k_{pol}]_{Q,d}}{[k_{pol}]_{Q,d=10cm}}$$

(1)

where M is the IC signal corrected for the influence quantities and normalized to the monitor units, $s_{w,air}$ is the water-to-air stopping power ratio at the depth of measurement (z_{max}), k_s is the correction factor for lack of charge collection due to the ion recombination effects and k_{pol} is the correction factor for polarity effects. $s_{w,air}(z_{max})$ and k_{pol} were determined according to the IAEA TRS-398 dosimetry protocol [14], while the modified TVA method that includes the free-electron component was applied for determining k_s, as proposed by Laitano et al. [17]. According to this method, k_s for the polarizing voltage V_1 can be determined using the third Boag's model:

$$k_s''' = \left[\lambda_1 + \frac{1}{u_1} ln \left[1 + \frac{e^{\lambda_1(1-\lambda_1)u_1} - 1}{\lambda_1} \right] \right]^{-1}$$

(2)

with $\lambda = 1 - \sqrt{1-p}$ and, p the free-electron fraction. The parameter u_1 was obtained by numerically solving the equation:

$$\frac{M_1}{M_2} = \frac{\lambda_1 u_1 + ln \left[1 + \frac{1}{\lambda_1} \left(e^{\lambda_1(1-\lambda_1)u_1} - 1 \right) \right]}{\lambda_2 u_1 + \frac{V_2}{V_1} ln \left[1 + \frac{1}{\lambda_2} \left(e^{\lambda_2(1-\lambda_2)\left(\frac{V_1}{V_2}\right)u_1} - 1 \right) \right]}$$

(3)

where M_1 and M_2 are the IC signals obtained with polarizing voltage V_1 and V_2, corrected for polarity effect and normalized to the monitor units. The free electron fraction at each polarizing voltage was determined according to Laitano et al. [17] using nominal values of the ionization chamber electrode spacing.

2.3. Alanine/EPR dosimetry

Alanine pellets used in this work were provided by Gamma-Service (Leipzig, Germany). They consist of 96% by weight of alanine and 4% of binder material. Pellets are cylindrically shaped with diameter of (4.80 ± 0.04) mm, height of (2.98 ± 0.04) mm and mass of (64.5 ± 0.5) mg. The density of the pellets is about 1.2 g cm^{-3}. Alanine dosimeters were calibrated in terms of absorbed dose to water in a reference ^{60}Co beam at the Italian Primary Standard Dosimetry Laboratory (ENEA-INMRI). Calibration doses were in the range 7–13 Gy with a relative uncertainty of 0.6% (k = 1).

For alanine measurements a Bruker ELEXSYS spectrometer (Karlsruhe, Germany) operating in the X-band and equipped with a Bruker SHQ cavity was used. Spectra were recorded using the following EPR parameters: sweep field, 2.5 mT; modulation amplitude, 1 mT; microwave power, 2 mW; scan time, 20 s; time constant, 320 ms.

For EPR reading, 3 alanine pellets (hereinafter referred to as dosimeter), irradiated in the same experimental conditions, were arranged in a vertical stack and measured simultaneously as described elsewhere [35]. Each dosimeter was inserted in a quartz tube and placed in the EPR cavity for reading. The mean value of the peak-to-peak amplitude of the central peak of the alanine spectra of three EPR measurements is taken as dosimeter response. Between two successive measurements the stack is taken out and randomly repositioned in the quartz tube. Three averaged scans are taken for each EPR spectrum acquisition.

During the measurement session, stability of the EPR spectrometer was checked measuring a reference dosimeter, consisting of a 100 Gy irradiated alanine dosimeter, sealed in a quartz tube and stored in the dark at laboratory conditions. Temperature and humidity in the laboratory were under controlled conditions. However a dosimeter (a

stack of 3 pellets) belonging to the calibration set, kept in the same conditions as the dosimeters to be measured, was also periodically checked during the measurement session to monitor the signal variations due to changes in the environmental conditions.

As irradiation temperature affects the alanine response, a correction was applied to take into account for any temperature deviation from the calibration conditions. Additionally, according to Zeng et al. [36], a correction for the radiation quality dependence of alanine response in electron beams relative to ^{60}Co was applied. Specifically, an increase of 1.3% in the alanine signal was considered. No other correction was applied. The combined standard uncertainty in the alanine dose assessment is 1% (k = 1). It is estimated by combining in quadrature the uncertainties in the calibration dose, in the alanine dose evaluated as prediction interval and in the stability of the spectrometer.

For purpose of measuring the OFs, a PMMA holder was used consisting of a plate containing 3 contiguous cylindrical holes, each hosting a single alanine pellet. The layer of PMMA over the pellets facing the beam direction is about 150 μm. A PMMA cover, provided with an O-ring seal, keeps the pellets in the right position and protects them from humidity when irradiations are performed in water. Two repeated irradiations, with the same nominal absorbed dose to water, were performed in each experimental configuration.

3. Results

3.1. Beam characteristics

The PDD curves obtained by means of the PTW 60017 diode showed no significant change with applicator diameters in the range 4–10 cm, except for a slight increase of the percentage dose in the surface region. Fig. 1 shows PDD curves for the reference (10 cm) and the smallest applicator diameter (4 cm) at 7 and 9 MeV. Since no significant shift in the depth of maximum dose was observed decreasing the applicator size, for each energy OF measurements were made at the same depth for all applicators (e.g. 1.3 cm and 1.2 cm for 9 MeV and 7 MeV, respectively). The beam quality index, R_{50}, resulted 3.05 cm and 2.59 cm for the 9 MeV and 7 MeV beams, respectively. Lateral dose profiles showed a good beam homogeneity (see Fig. 2) with beam non-uniformity effects over the different detector sensitive volumes within 0.2%. The dose per pulse measured by alanine dosimeters ranged from 34 to 75 mGy for the 9 MeV beams and from 29 to 63 mGy for the 7 MeV beams.

3.2. Ionization chambers characterization

Fig. 3 shows $1/M$ versus $1/V$ plots for all the ICs used in this work in the polarizing voltage range from 50 V to 400 V. Linear fits to the measured data are also shown in Fig. 3. R^2 values ranged from 0.995 to 0.999 thus confirming that the adopted operating voltage, V_1 in Table 1, is in the linearity range for all the ICs.

Concerning the polarity effects, variations in k_{pol} factor with polarizing voltage and applicator diameter were found within 0.3% except for the Markus IC that also exhibited the largest polarity effects. In the reference field size, varying the polarizing voltage from 400 V to 50 V the Markus k_{pol} value changed from 1.016 to 1.028, for both electron beam energies. Moreover, for this IC the k_{pol} value increased with decreasing beam size. At 400 V operating voltage, the k_{pol} obtained for the 10 cm and 4 cm applicators differed from each other about 2%. For the other ICs polarity effects were generally below 0.5%.

For each ionization chamber reported in Table 1, the corresponding k_s factors obtained at the lowest and the highest dose per pulse used in this work are shown in Table 2. For the PPC05 and the Adv.Markus k_s values are comparable to the values currently obtained in conventional radiotherapy beams. Variations of k_s with the applicator diameter are negligible for the PPC05 and proved to be below 0.6% for the Adv.Markus. Correction factors for the other IC types always exceed the limit of 1.05 reported in the dosimetry protocols [14,15] with k_s
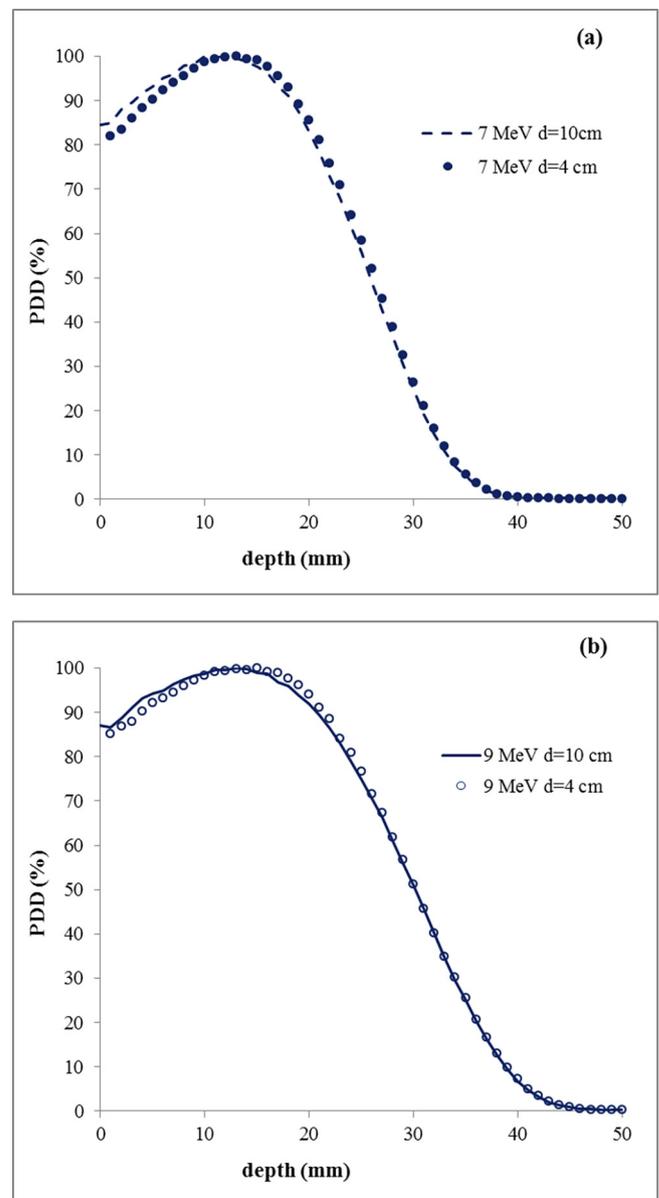

Fig. 1. 7 MeV (a) and 9 MeV (b) percentage depth dose curves for applicators with diameter 10 cm (lines) and 4 cm (circles).

varying of several percent (up to about 11%) with the applicator diameter.

3.3. Output factors

Output factors obtained by means of ionization chambers, diodes and microDiamond (hereinafter referred to as OF_{det}) are shown in Table 3 for the applicator diameters and the two nominal energies considered in this work. Reference values for the output factors (OF_{ref}) determined by means of alanine dosimeters, under the assumption of energy independence of the dosimeter response on dose per pulse and electron beam energy [24,33,34], are also reported in Table 3. The agreement between OF_{det} and OF_{ref} is given in terms of percentage difference (values in brackets in Table 3):

$$\Delta_{det} = 100 * \left(\frac{OF_{det}}{OF_{ref}} - 1 \right) \tag{4}$$

The standard deviation of alanine measurements normalized to the accelerator monitor units was 0.5% for the reference applicator and
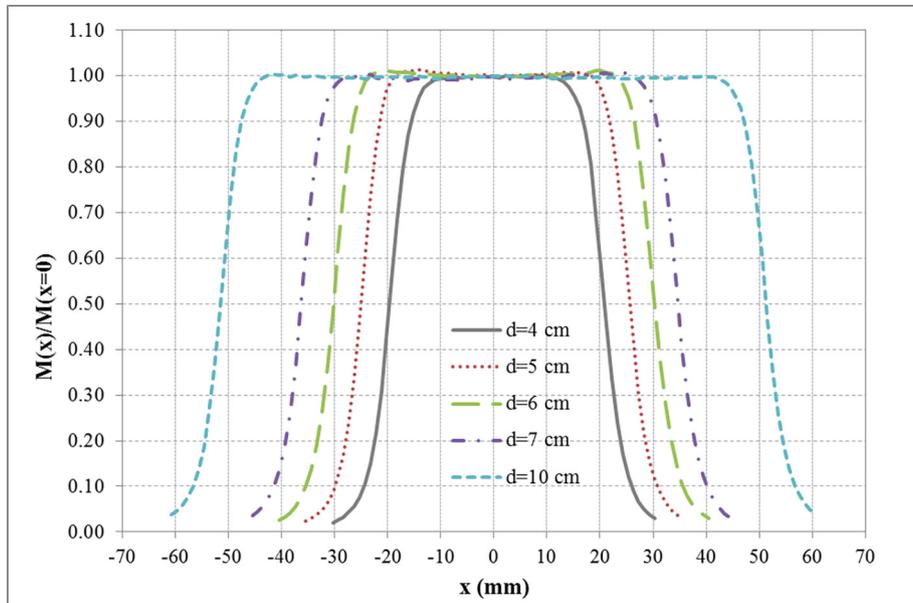
Fig. 2. Lateral beam profile for 7 MeV electron beams collimated by applicators with diameter 10–7-6–5 and 4 cm.

ranged from 0.2% to 0.7% for the other applicators. Considering a long-term reproducibility of the accelerator relative output of 0.7% (1σ), a combined standard uncertainty of 0.8% is associated to the OF_{ref} values.

Standard deviations of charge measurements normalized to the monitor units were 0.2% for the ICs and 0.3% for the solid-state detectors (i.e. diodes and microDiamond). Therefore, considering the above-mentioned 0.7% reproducibility in the accelerator relative output, the combined standard uncertainty of OF_{det} for ICs and solid-state detectors is 0.7% and 0.8%, respectively. Such figures do not include uncertainties in k_s determination for the ICs. Furthermore the following assumptions are made: dose-rate independence of solid-state detectors and negligible uncertainty in the position of the effective point of measurements for all the detectors.

With reference to Table 3, OF_{ref} values ranged from about 1.8 (applicator diameter 7 cm) to about 2.2 (applicator diameter 4 cm) and showed similar trend with applicator diameter for both the nominal

beam energies. Concerning OF_{det} results, the agreement among solid-state detectors was better than 1.5% except for the 6 cm applicator at 7 MeV, for which a maximum difference of 1.9% was obtained between microDiamond and PTW 60017 diode. Differences among OF_{det} values obtained by the various types of ICs were generally larger than 1.5% with a maximum value of 2.6% obtained for the 6 cm applicator at 9 MeV between PPC40 and Markus ICs.

OF_{det} values relative to OF_{ref} are shown in Fig. 4 for the solid-state detectors and in Fig. 5 for the ionization chambers. The dashed lines in Figs. 4 and 5 indicate the 95% confidence interval of OF_{det}/ OF_{ref} based on the expanded uncertainty of alanine measurements (1.6%, k = 2). Both figures show good agreement with alanine, almost all data being within the 95% confidence interval of alanine results. For the PTW 60017 silicon diode and the PTW 60019 microDiamond the agreement with alanine was better than 1% for the 9 MeV, while deviations were typically larger at 7 MeV, with values up to about 2% for the 4 cm and
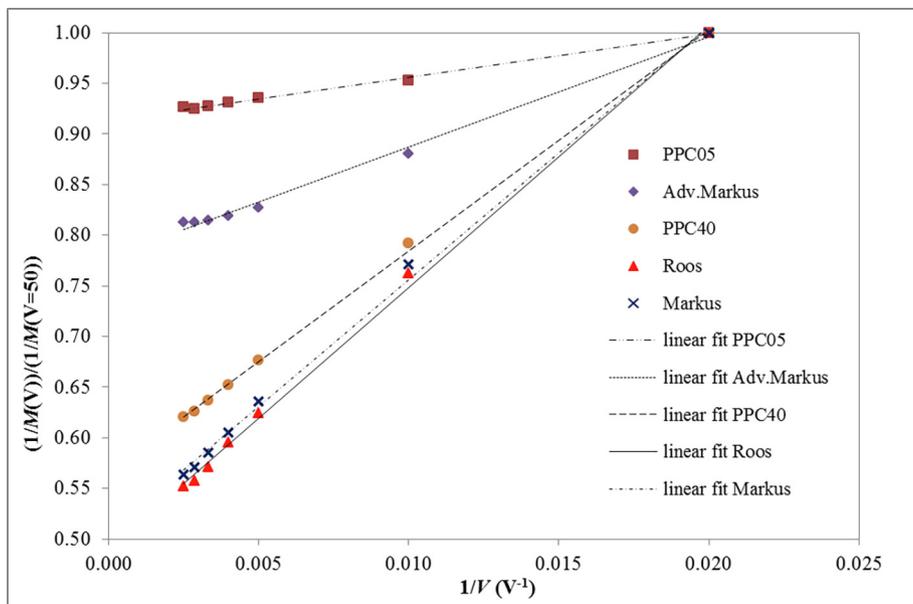

Fig. 3. Plot of reciprocal of chamber signal ($1/M$) versus reciprocal of polarizing voltage ($1/V$) for the Advanced Markus, the Markus, the PPC05, the PPC40 and the Roos plane-parallel ionization chambers. The $1/M$ values are normalized to the value obtained with the lowest polarizing voltage (50 V).

Table 2
Correction factors for ion recombination effects, k_s, at the lowest and highest dose per pulse (DPP) values, obtained with the 10 cm and 4 cm applicator diameter, for the 7 MeV and 9 MeV nominal electron energies. For all the ionization chambers k_s values were determined for the operating voltage V_1 using the modified two-voltage method based on the third Boag's model [17], with voltage ratio V_1/V_2.

Chamber type	V_1 (V)	V_1/V_2	k_s			
			7 MeV		9 MeV	
			d = 10 cm; DPP 29 mGy	d = 4 cm; DPP 63 mGy	d = 10 cm; DPP 34 mGy	d = 4 cm; DPP 75 mGy
PPC05	300	3	1.001	1.002	1.002	1.003
Adv.Markus	400	4	1.004	1.009	1.005	1.011
Markus	400	4	1.066	1.126	1.078	1.146
Roos	400	4	1.067	1.138	1.080	1.167
PPC40	300	3	1.090	1.188	1.110	1.228

5 cm applicators. The agreement between ionization chambers and alanine was within 1.1% with a few exceptions regarding the Markus, the PPC40 and the Roos ICs.

4. Discussion

Electron beams generated by some mobile accelerators dedicated to intraoperative radiotherapy are characterized by dose per pulse values more than 10 times larger than those of conventional beams, thus posing problems for both reference and relative dosimetry. For the Novac7 IORT accelerator considered in this work the dose per pulse was around 30 mGy per pulse (10 Gy min^{-1}) using the reference applicator and increased up to 75 mGy per pulse using clinical applicators. It is well known that at dose per pulse higher than 10 mGy the use of ionization chambers for absorbed dose measurement is limited by the high density of electric charge in the air cavity. The current consensus is that methods alternative to those recommended in the dosimetry protocols to determine the ion recombination correction factors are required. The Novac7 dose rates might be potentially critical even for on-line solid-state detectors, since for some types of such detectors a dose rate dependence has been reported in literature at dose rates typical of conventional beams. Against this backdrop, our work focused on assessing the suitability of several types of ionization chambers and on-line solid-state detectors for output factor measurements through comparison with alanine dosimeters, whose response is independent of dose rate. The PTW Adv.Markus, Markus and Roos ICs, the IBA PPC40 and PPC05 ICs, the PTW 60017 and the IBA EFD^{3G} electron silicon diodes and the PTW 60019 microDiamond were considered.

For the silicon diodes and the microDiamond very good results were obtained. Both for 7 and 9 MeV energy, OFs$_{det}$ measured using the three solid-state detectors typically agree within ± 1%. The same level of agreement (below ± 1%) was obtained when such OFs were compared to alanine at 9 MeV. At 7 MeV deviations of OFs$_{det}$ from alanine were larger, especially for the smallest applicators. However, almost all data were within the 95% confidence interval of the alanine measurements

(Fig. 4). The only exceptions were OFs obtained by the PTW 60017 diode with the 4 cm applicator and the microDiamond with applicator size 5 cm, both deviating 2% from alanine results. Considering that for these detectors the uncertainty of OF$_{det}$ was estimated to be 0.7% (1σ), a deviation of 2% is still consistent with the combined expanded uncertainty of Δ_{det} (2.1%, k = 2). It should be noted that no corrections were applied to the detector signals when determining OF$_{det}$. Data in Fig. 4 for the 7 MeV beams, by contrast, show a tendency of OF$_{det}$/OF$_{ref}$ to increase with reducing field size, possibly indicating an increase of detector response with (increasing) dose per pulse. However such a tendency is not confirmed by data at 9 MeV. Importantly, since the changes in dose rate with applicator diameter is approximately the same for the two energies it can be concluded that our data do not support any significant dose rate effect on OF$_{det}$ determination.

With respect to ionization chambers, considering the reproducibility of IC signals (0.2%, 1σ) and accelerator relative output (0.7%, 1σ), differences among OF$_{det}$ measured for two ICs are deemed acceptable up to 2% (k = 2). Table 3 proves that differences exceeding 2% were obtained in a number of instances, thereby suggesting that additional uncertainty components need to be considered in the final uncertainty budget. In this regard, it is worth noting that OFs$_{det}$ determined by Eq. (1) include corrections accounting for variations of k_s and k_{pol} with applicator diameter. Corrections related to polarity effects were generally below 0.3%, thereby with marginal effects on OF$_{det}$ determination. On the contrary, variations in k_s with field size were in the range 4%–11% for the Markus, the PPC40 and the Roos ICs, thus significantly affecting the corresponding OF$_{det}$ values. k_s variations were smaller for the PPC05 and the Adv.Markus (i.e. below 0.1% and 0.6%, respectively). On the other hand differences between OFs$_{det}$ measured with these two ICs were always within ± 0.6%, therefore well within the stated uncertainty of 2% (k = 2).

We determined k_s by Eq. (2) using the modified TVA method proposed by Laitano et al. [17]. According to those authors a standard uncertainty of 2% should be associated to k_s values. However, since k_s values for two different applicators are correlated to some extent, a

Table 3
Output factors for the Novac7 electron beams determined by ionization chambers, silicon diodes and diamond detector (OF$_{det}$), and reference values determined by alanine dosimeters (OF$_{ref}$). In brackets the percentage differences Δ_{det} (see Eq. (4)).

| Applicator diameter	7 MeV				9 MeV			
	7 cm	6 cm	5 cm	4 cm	7 cm	6 cm	5 cm	4 cm
Adv.Markus	1.803 (< 0.1%)	1.958 (−0.3%)	2.087 (0.5%)	2.174 (0.3%)	1.799 (0.4%)	1.963 (1.1%)	2.108 (−0.1%)	2.227 (1.1%)
Markus	1.811 (0.5%)	1.950 (−0.7%)	2.078 (0.1%)	2.137 (−1.5%)	1.780 (−0.6%)	1.931 (−1.5%)	2.078 (−1.5%)	2.187 (−0.7%)
PPC05	1.809 (0.3%)	1.946 (−0.9%)	2.099 (1.1%)	2.183 (0.7%)	1.799 (0.4%)	1.951 (0.5%)	2.119 (0.5%)	2.224 (1.0%)
PPC40	1.819 (0.9%)	1.979 (0.8%)	2.100 (1.1%)	2.137 (−1.5%)	1.810 (1.1%)	1.982 (2.1%)	2.123 (0.7%)	2.228 (1.1%)
Roos	1.812 (0.5%)	1.942 (−1.1%)	2.099 (1.1%)	2.134 (−1.6%)	1.806 (0.8%)	1.942 (< 0.1%)	2.117 (0.4%)	2.223 (0.9%)
EFD^{3G}	1.811 (0.4%)	1.958 (−0.3%)	2.108 (1.5%)	2.201 (1.5%)	1.804 (0.7%)	1.958 (0.9%)	2.101 (−0.4%)	2.230 (1.2%)
PTW 60017	1.820 (1.0%)	1.970 (0.3%	2.107 (1.5%)	2.213 (2.0%)	1.777 (−0.8%)	1.938 (−0.1%)	2.099 (−0.5%)	2.209 (0.3%)
PTW 60019	1.794 (−0.5%)	1.933 (−1.6%)	2.117 (2.0%)	2.192 (1.1%)	1.792 (< 0.1%)	1.945 (0.2%)	2.097 (−0.5%)	2.218 (0.7%)
Alanine	1.803	1.964	2.076	2.169	1.791	1.941	2.109	2.203
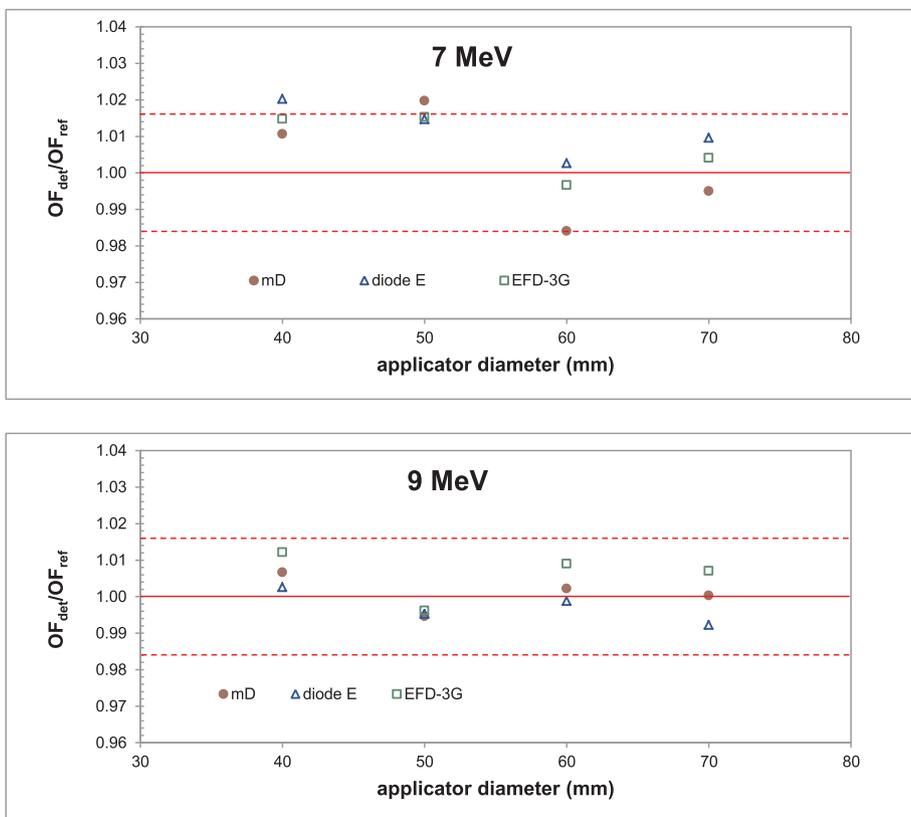
Fig. 4. Output factors determined by the solid state detectors (OF$_{det}$) relative to the reference output factors (OF$_{ref}$) determined by alanine dosimeters. The dashed lines indicate the 95% confidence interval of alanine measurements.

Fig. 5. Output factors determined by ionization chambers (OF$_{det}$) relative to the reference output factors (OF$_{ref}$) determined by alanine dosimeters. The dashed lines indicate the 95% confidence interval of alanine measurements.
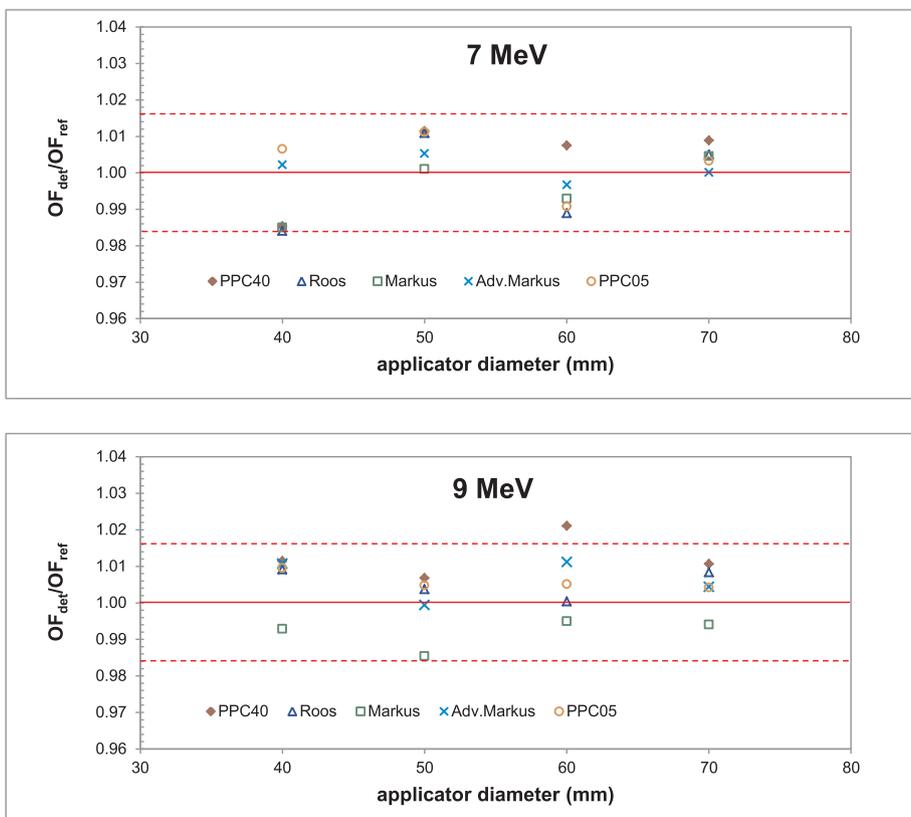
standard uncertainty of 1% in their ratio seems a reasonable estimate [30]. As a consequence, combining this standard uncertainty (1%) with those mentioned above (0.7% accelerator output and 0.2% IC signal), a combined standard uncertainty of 1.4% can be ultimately associated to the OF_{det} determined by ionization chambers. According to such estimate, the combined standard uncertainty in the ratio of OF_{det} between two different ICs is 2%. Therefore, for a given applicator size and beam energy, all IC data reported in Table 3 are in agreement within the stated expanded uncertainty (4%, k = 2).

Fig. 5 compares OFs between ionization chambers and alanine. All IC OFs are within the 95% confidence interval of alanine measurements except for the OF_{det} obtained by the PPC40 at 9 MeV, 6 cm applicator size, that deviates from the reference value by 2.1%. Such deviation is acceptable, if the 1.4% uncertainty of OF_{det} derived above is included in the uncertainty budget. Note that the best agreement with the alanine results was obtained for the Adv.Markus and the PPC05 ICs with Δ_{det} ranging from −0.3% to 1.1% and from −0.9% to 1.1%, respectively.

Our findings suggest that variations in ion recombination effects can strongly affect the OF determination. As a consequence, the accuracy of OF values strictly depends on accuracy in k_s determination. OFs_{det} in this work were determined using k_s values derived from the third Boag's model including the free electron component. However, for absorbed dose measurements at high dose-per-pulse, some authors have indicated the first Boag's model as the most appropriate for k_s determination [37] as well as the traditional TVA method has been recently suggested as appropriate for measurements by the Adv.Markus IC up to 35 mGy per pulse [27]. With this in mind, we evaluated the impact of different approaches for k_s determination on OF results. In particular, we considered the three Boag's models and the traditional TVA method. Table 4 reports the minimum and maximum percentage differences between OF_{det} and OF_{ref} for the various k_s determinations. We note from Table 4 that for the PPC05, all three Boag's models provide output factors in agreement with alanine within approximately ± 1%. For the Adv.Markus the same three models provide results within the 95% confidence interval of alanine measurements (Δ_{det} values from −0.5% to 1.5%). For the Markus, the first and the third Boag's model give results well in agreement with alanine, while the second model leads to a significant underestimation of OF_{det} ($[\Delta_{det}]''$ values from −0.4% to −2.6%). Ultimately, for the PPC40 and the Roos ICs, the third Boag's model provides the best agreement with alanine, while the first and second models tend to overestimate (up to 3.8%) and underestimate OFs (down to −2.9%), respectively.

Concerning the traditional TVA method, OF values are systematically overestimated for all the ICs. Percentage differences from the alanine OFs are generally larger than 5% and in some cases than 10%. For the PPC05 the differences are below 2% but it should be noted that this IC exhibits very small ion recombination effects when polarized at 300 V (see k_s values in Table 2).

The most striking result to emerge from the data in Table 4 is that despite the first and the second Boag's models providing satisfactory correction factors for some ICs, the adoption of the third Boag's model ensures accurate OF results for all the ICs. Furthermore our results are

consistent with previous results, indicating that the traditional TVA method should be avoided to assess k_s factors, even for the measurement of relative outputs.

Importantly, our results share a number of similarities with previous literature findings [25,30,37,38], detailed hereafter. In particular our findings for Adv.Markus and Markus ICs are in line with data reported by Cella et al. [37] who used Fricke dosimeters as reference. In their study output factors determined using the three Boag's models were generally in agreement with Fricke results within 2% for both ICs. However, for the Markus IC the use of the second Boag's model underestimates OFs by 3%, approximately. In Marrale et al. [25] OFs obtained by Markus IC using k_s determined by the third Boag's model deviated from alanine measurements from −2.3% to −3.5%. Our data confirm tendency of the Markus IC to underestimate the OF, although deviations never exceed −1.5%. The larger deviations reported by Marrale et al. are justified by the 3% uncertainty of their alanine measurements. In another study, Iaccarino et al. [38] performed OF measurements on a LIAC accelerator using Adv.Markus and PPC05 ICs. They found an agreement between the two ICs typically below 1%, thereby correlating favourably with our data, reported in Table 3. Finally, a comparison between Adv.Markus and microDiamond has been made by Di Venanzio et al. [30] in IORT beams produced by a NOVAC11 accelerator with dose per pulse up to 100 mGy. OFs measured by the microDiamond generally agree with the Adv.Markus results within 1% with a maximum deviation of 1.9%. The same level of agreement was found in the present study (Table 3).

5. Conclusions

Our work has led us to conclude that all the detectors considered in this work can be used to measure OFs in high dose-per-pulse electron beams with an accuracy below 2% (k = 1). For the PTW 60017 and the IBA EFD[3G] electron silicon diodes and the PTW 60019 microDiamond OFs can be determined as the ratio of detector signals, with no need for any correction. On the other hand, OF measurements by ionization chambers require corrections to take into account variations in water-to-air stopping power values, polarity and ion recombination effects with beam size. In particular, attention should be paid to correctly determine the ion recombination correction factors, k_s, that might vary by several percent between the reference and the clinical field size. We have provided further evidence that the third Boag's model is the most accurate in correcting for ion recombination, providing OFs in good agreement with alanine for all types of ionization chambers considered in this work. On the other hand, our study confirms that the traditional TVA method fails to describe the variation of k_s with the field size in high dose-per-pulse beams causing unacceptable OF overestimations.

Table 4

Minimum and maximum percentage differences between ionization chambers and alanine output factors (see Eq. (4)) obtained applying different methods for k_s determination. $[\Delta_{det}]^{TVA}$ refers to the traditional two-voltage-analysis method [14], $[\Delta_{det}]'$, $[\Delta_{det}]''$, and $[\Delta_{det}]'''$ refer to the first, the second and the third Boag's model [17], respectively.

	$[\Delta_{det}]^{TVA}$		$[\Delta_{det}]'$		$[\Delta_{det}]''$		$[\Delta_{det}]'''$	
	Min	Max	Min	Max	Min	Max	Min	Max
Adv.Markus	2.1%	5.2%	0.0%	1.5%	−0.5%	0.9%	−0.3%	1.1%
Markus	4.9%	7.1%	−0.2%	1.4%	−2.6%	−0.4%	−1.5%	0.4%
PPC05	−0.4%	1.7%	−0.9%	1.2%	−1.0%	1.1%	−0.9%	1.1%
PPC40	5.0%	8.9%	0.0%	3.8%	−2.8%	0.7%	−1.5%	2.1%
Roos	6.0%	11.0%	−0.1%	2.9%	−2.9%	−0.2%	−1.6%	1.1%

Conflicts of interest

None.

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