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Original research article

In vivo dosimetry of the rectum in image-guided adaptive interstitial-intracavitary brachytherapy of cervix cancer – A feasibility study

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ARTICLE INFO

Article history:
Received 9 October 2018
Accepted 27 January 2019
Available online 14 February 2019

Keywords:
In vivo
Dosimetry
Rectal dose
Cervical cancer
Interstitial brachytherapy

ABSTRACT

Aim and background: To investigate the feasibility of in vivo rectal dosimetry in image-guided adaptive brachytherapy of cervical cancer.
Materials and methods: Error of measurement of dose rate in a semiconductor diode probe was investigated depending on the distance and angle in water, and on temperature in a polymethyl methacrylate phantom using an Ir-192 source. Furthermore, the difference between the measured and calculated dose was analysed in the interstitial brachytherapy of 30 cervix cancer patients. The relationship between in vivo measured dose, calculated dose in the point of the diode, calculated maximal dose in the point of the diodes and calculated maximal dose of the rectum were examined.
Results: The dosimeter measured with 85% accuracy at more than 5 cm from the source, but within a closer distance the accuracy decreased significantly. At 45–90° angle, the device measured with a 15% error. The error increased with the temperature, 22% at 35 °C. In 8 cases (26.7%) the maximal dose was measured in the correct diode. The device measured 73% of the calculated dose in the point of the diode. The maximum of the calculated doses of diodes was 60% of the calculated maximal dose. The in vivo measured dose was 35% of the calculated maximal dose.
Conclusions: Under treatment conditions, the semiconductor diode does not provide reliable measured data. The probe pushes the rectal wall closer to the high dose areas and underestimates the dose of it. Semiconductor probe is not recommended for in vivo dosimetry of the rectum in image-guided brachytherapy of cervical cancer.

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https://doi.org/10.1016/j.rpor.2019.01.004

1. Background and aim

The standard of care in brachytherapy (BT) of cervical cancer is image-guided adaptive intracavitary (ic.) or interstitial (is.) treatment technique.[1–4] Accurately accomplished implantation, dose planning and dose reporting have an essential rule within the striving after dose escalation.[5,6]

Several dose–volume parameters show correlation with tumour control and side effects. The dose coverage of the target volume (D90, the minimum dose delivered to 90% of the High-Risk Clinical Target Volume – HR-CTV) correlates with local tumour control,[5,7,8] and the minimal dose of the most exposed 2 ccm of the OARs with normal tissue toxicity.[2,9] Beside the calculated parameters, in vivo dose measurement also has been used in clinical routine for independent dose verification.[10] It is an important point when high doses are given in a treatment fraction, but the task is challenging because of the high dose gradient, especially close to the radioactive source.

Several in vivo measurement techniques have spread for quality assurance. Ionisation chambers and solid state detectors are limited in their usefulness for near-catheter dosimetry because of their physical size and dose rate dependence. Gafchromic film has an advantage of a large dose–response range, excellent spatial resolution, and near energy independence for megavoltage photons, but it is not applicable inside patient's body.[11] The thermoluminescent detectors (TLD) cannot provide real time readings and have depth dependent sensitivity.[12,13] The Metal Oxide Semiconductor Field Effect Transistor (MOSFET) has an accuracy of 5% for distances of 20–50 mm from the Ir-192 source in water but gave errors of 30–40% for distances greater than 50 mm from the source.[13,14]

Fibre optic scintillation dosimeters (PSD), consisting of a plastic scintillator coupled to an optical fibre, are among the most promising dosimeters for this application. They have external diameters of 2.2 mm and 1 mm that can be easily inserted into catheters or arranged around applicators. The background signal created by Cerenkov and fibre fluorescence does not significantly affect the performance in most clinical geometries using an Ir-192 source from an HDR brachytherapy unit.[15] Unfortunately, at present, there are no PSD systems that are commercially available for use for in vivo dosimetry in BT. The only PSD system available commercially was designed for external beam radiotherapy and, more specifically, for the characterisation of small field dosimetry.

Semi-conductor diodes (SCD) are used to avoid misadministrations of delivered dose and large scale dosimetric mistakes. Their advantages are on-line readout, high sensitivity, good spatial resolution, simple instrumentation, minimal energy dependence and absence of bias voltage. Alecu et al.[16] evaluated brachytherapy treatments of 19 patients with cervical cancer using four SCDs in the rectum. They found that the maximum discrepancy between the measured and calculated dose values in diodes was 15%; however, they used only two orthogonal X-ray images for dose calculation and neglected the anatomy of the rectum and the used internal shielding.

Waldhaüsl et al.[17] measured the doses in the rectum and bladder in 55 applications and compared them to the computed doses. Differences were ranging from −31 to +90% (mean 11%) for the rectum and from −27 to +26% (mean 4%) for the bladder. They did not use 3D planning, calculated the dose only for the ICRU reference points of the rectum and bladder. They found that the dose was underestimated with in vivo SCDs ranging from −61 to 156% (mean 29%) for the rectum and from 12 to 162% (mean 58%) for the bladder.

The aim of the present study is to evaluate the dosimetric uncertainty using semiconductor diodes in image-guided adaptive high-dose-rate BT of cervical cancer.

2. Materials and methods

First, the dosimetric characteristics of a 5-diode semiconductor (Silicium) dose metre (PTW T9112, Freiburg, Germany) (Fig. 1) were determined. The diodes are connected to a dedicated multichannel electrometer (PTW Multidos T10004, Freiburg, Germany) for direct signal display and dose-rate was measured. The calibration for each individual diode was performed under reference conditions – at 8 cm distance from the Ir-192 source, in parallel with the axis of the source, in room temperature (22.5 °C) water.

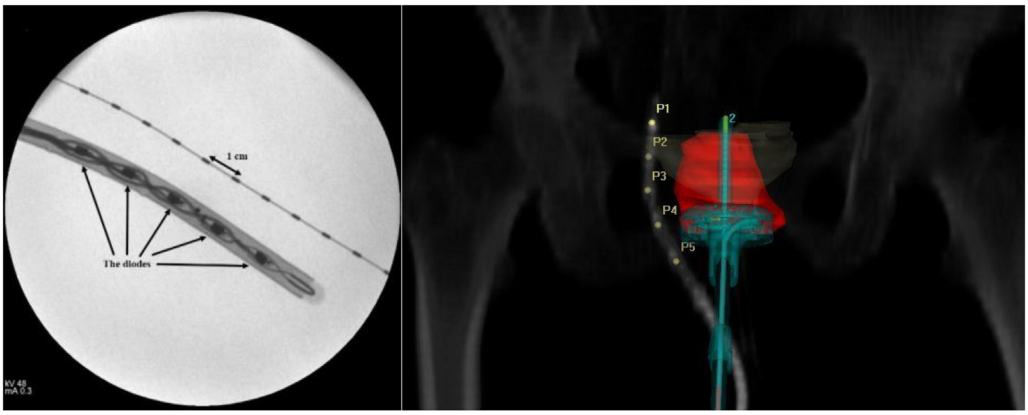

Fig. 1 – (a) The in vivo probe with 5 semiconductor detectors in an X-ray image (left). (b) The in vivo probe in a 3D reconstructed image. P1–5: detectors, an intracavitary applicator is in the target volume. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

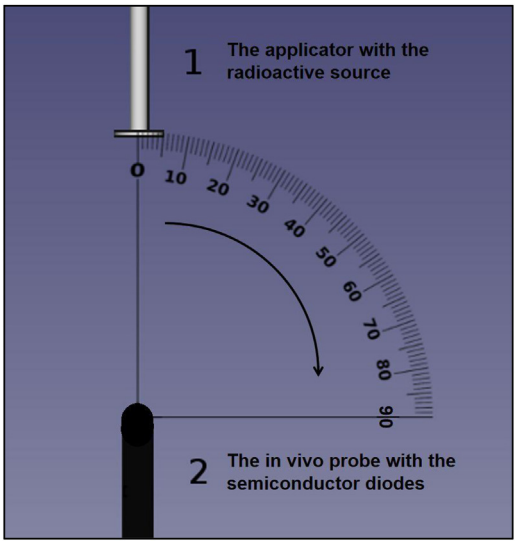

Fig. 2 – Configuration of angular dependence measurement.

Distance dependence: a one-channel BT applicator was fixed and the diode was moved from 5 to 100 mm from the source dwell position with the step size of 5 mm. The angle between the axis of the source and the diodes was 90° (Fig. 2).

Angular dependence: in the same configuration, the axis of the source was rotated around the axis of the diode from 0 to 90° with a 5° step size at 80 mm distance from the diode (Fig. 2). Both of the distance and angular dependence measurements were performed in water with 22.5 °C temperature.

Temperature dependence: both the applicator and the dosimeter were placed in a water equivalent polymethyl methacrylate phantom apart of 80 mm from each other perpendicularly. The temperature of the phantom was increased from 20 to 40 °C with a 5 °C step size.

Every measurement was repeated three times, and the ratio of the mean of the measured dose and computed delivered dose was calculated (measured-to-delivered ratio, MDR) in each configuration.

In the second part of our study, 30 interstitial-intracavitary CT-based BT treatment of cervical cancer was selected. Calculated dose of the diode where the device measured the maximal dose (CDD), calculated dose of the most irradiated diode in the plan (CDMD), calculated volumetric maximal dose (the minimal dose of the most exposed 0.1 ccm, D0.1) of the rectum and in vivo measured doses (IVMD) were compared with Spearman Rank Order Correlation, Friedman-ANOVA and Fisher-LSD (Least Significant Difference) post hoc test (Statistica 12.5, StatSoft, Tulsa, OK, USA).

3. Results

The measured-to-delivered dose ratio increased with the distance between the Ir-192 source and the diodes: at 5 mm it was 0.01, at 100 mm, 1. At 4 cm the MDR was 0.49, but above 5 cm it was between 0.86 and 1 (Fig. 3). The MDR varied hectically with the angle between the axes of the source and the diodes. Between 45° and 90°, the device measured MDR of 0.84–0.96, but in smaller angles the error of measurement was higher. In 15° diodes measured 46%, in 10°, 41% of the delivered dose (Fig. 4). The dosimeter measured the dose with a higher error with increasing temperature, the MDR was 0.82 between 20 and 25 °C and 0.78 at 35 °C (Fig. 5).

In 8 cases of 30 treatments (26.7%), the maximal dose was measured in the diode where the maximal dose was calculated in the plan. The device measured 73% (26–126%) of the CDD on average, the CDMD was 60% (18–100%) of the D0.1, the IVMD was 35% (16–63%) of the D0.1 in the rectum (Fig. 6). These differences were all significant ($p < 0.001$) as is seen in Fig. 7. The mean IVMD was 2.08 Gy (0.89–3.84 Gy) and correlated with CDD (3.5 Gy, 1.05–10.05 Gy; $r^2 = 0.63$), with CDMD (4.11 Gy, 1.08–10.05 Gy; $r^2 = 0.64$) and D0.1 (6.94 Gy, 1.92–15.6 Gy; $r^2 = 0.78$). The CDD, CDMD and D0.1 were in inverse correlation with the ratio of IVMD and CDD and with the ratio of IVMD and D0.1 ($r^2 = -0.54$–0.76). The mean distance between the source and the most exposed diode was 23.9 mm (12.4–52.5 mm) and was inversely proportional to the ratio of CDD and D0.1 ($r^2 = 0.64$) and with the ratio of IVMD and CDD ($r^2 = 0.67$).

4. Discussion

In vivo dose verification has a fundamental importance in BT, although dose measurement is difficult within a close distance to a high-dose-rate radioactive source. Silicon SCDs are used in in vivo dose verification of the rectum in cervix cancer BT. At present, there are no better alternatives,[11–14] with PSDs as the only possible competitors for that in the future.[15] Beside the known disadvantage of SCDs – in vivo usage is painful for patients with sore mucosa – light is thrown on new problems in the era of image-guided BT.

First, the presence of diodes makes contouring more difficult on CT images because of the scattering artefacts. Ambiguous information can lead to a higher target volume, which can cause higher dose to organs at risk. Also, it is well seen on CT images (Fig. 6) that the detector pushes the rectal wall to the ring (or ovoids) of the applicator from the posterior and inferior direction. Rectum moves to the position of the sigmoid whose tolerance dose is lower.

Furthermore, diodes measure the dose in the cave of the rectum, although the maximal dose develops in the rectal wall. So, SCDs do not measure the maximal dose of the rectum. Underestimation of the dose by diodes is a well-known problem. Alecu et al. found the measured dose to be 15% lower than the calculated one.[16] However, they used X-ray images without 3D anatomical information. Compared to this, we found the measured dose to be 27% lower than the calculated dose in the diode, on average. Waldhaüsl et al. reported a larger difference between in vivo measured and calculated dose for the ICRU reference points of the rectum, from −61 to 156%.[17] Both of our laboratory and clinical investigations confirmed it. Under treatment conditions – 20–30 mm, 0–10°, 37 °C – the measured dose was around 34% of the delivered dose. The in vivo measured dose was 35% of the calculated volumetric maximal dose in the rectum, on average.

The measured dose was in agreement with the delivered one only over the distance of 50 mm. However, the main minimal distance of the source and the diodes was 23.9 mm, where the diodes measured only 13% of the delivered dose. Closer to

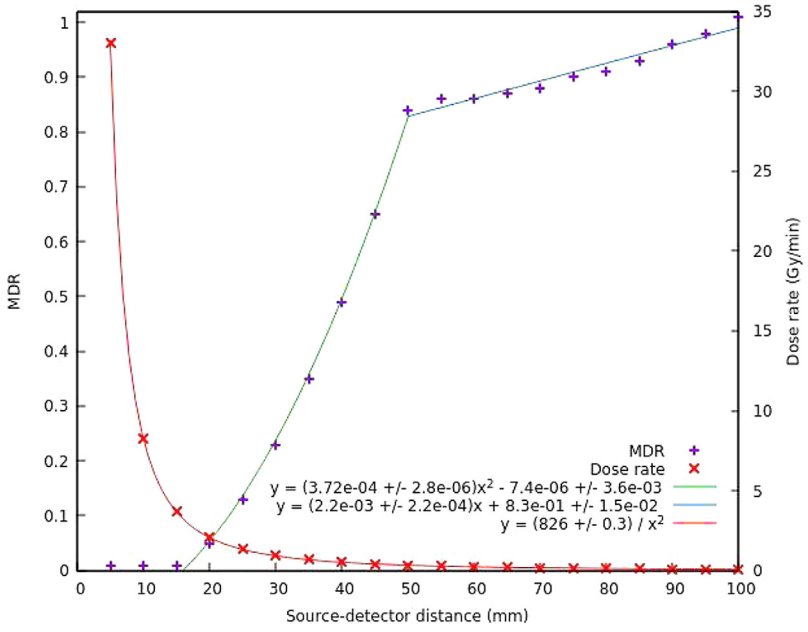

Fig. 3 – The measured-to-delivered dose ratio (MDR) and calculated dose rate depending on the distance between the source and the diode.

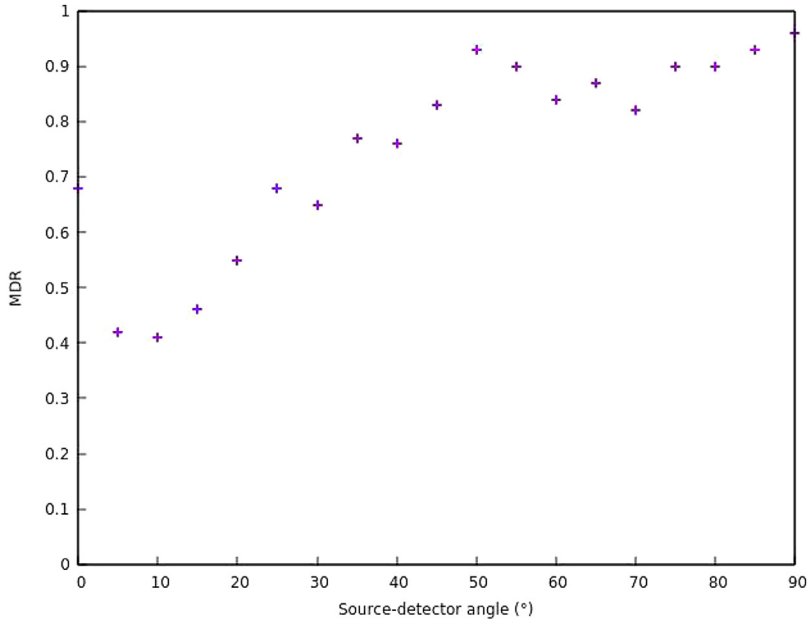

Fig. 4 – The measured-to-delivered dose ratio (MDR) depending on the angle between the axis of the source and the diode.

the source, the dose rate increases rapidly: 33 Gy/min at 5 mm. Although the maximal dose rate that this device is able to measure is 40 Gy/min,[18] the MDR is only 1% at the distance of 5 mm (Fig. 3). The angular dependence of the probe was not systematic. The highest agreement with the delivered dose was between the angles of 50° and 90°, but in patients this angle is usually 0–10°, where the MDR is 42%. In room temperature diodes measured 82% of the dose, and in human temperature only 78%.

The correlation analysis based on the in vivo measurements showed that higher doses were more underestimated by the SCD probe (CDD, CDMD and D0.1 was in inverse correlation with the ratio of IVMD and CDD and with the ratio of IVMD and D0.1). It is also clearly seen that the error of measurement is higher when closer to the radioactive source (distance between the source and the most exposed diode is inversely proportional to the ratio of IVMD and CDD), which supports the results of our laboratory measurement.

In the light of the above results, calculating dose–volume parameters of the rectum are the most accurate dose estimation method in image-guided brachytherapy of cervical cancer. For quality control, a priori checking methods (i.e. calculating TRAK or total treatment time) are more accurate than in vivo dosimetry. Without 3D imaging, SCD in vivo dosimetry is the

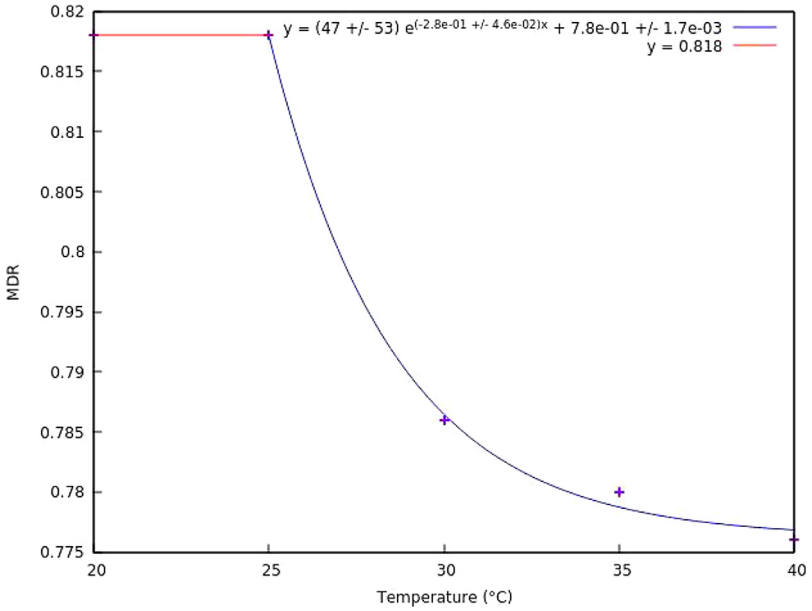

Fig. 5 – The measured-to-delivered dose ratio (MDR) depending on the temperature of the phantom.

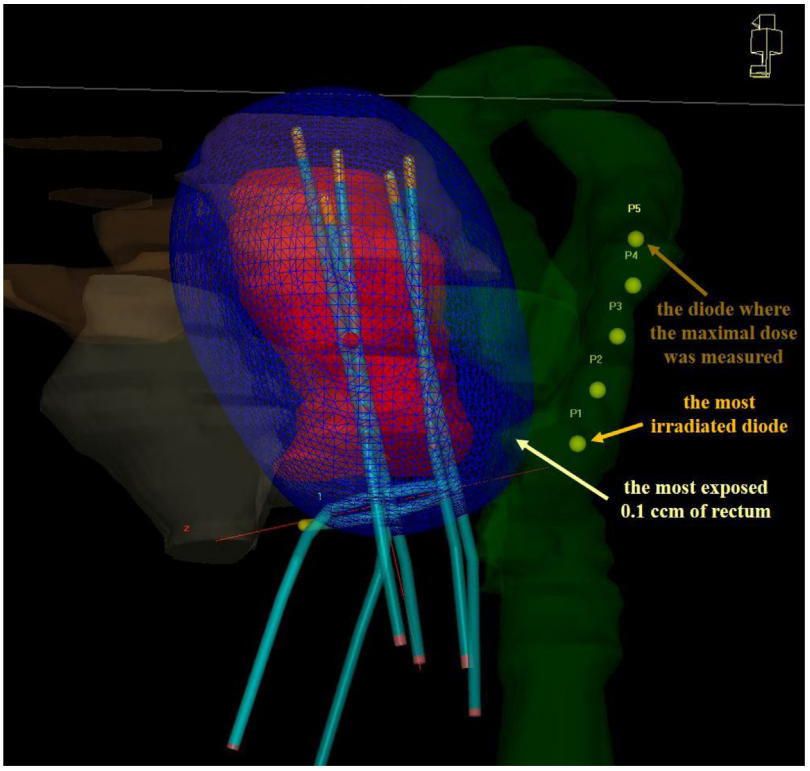

Fig. 6 – 3D reconstruction of the target volume (red), the bladder (yellow), bowels (brown), the rectum (green), the interstitial-intracavitary applicator (light blue), the surface of the dose of the most exposed 0.1 ccm (D0.1) of the rectum (dark blue) and the diodes (yellow points). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

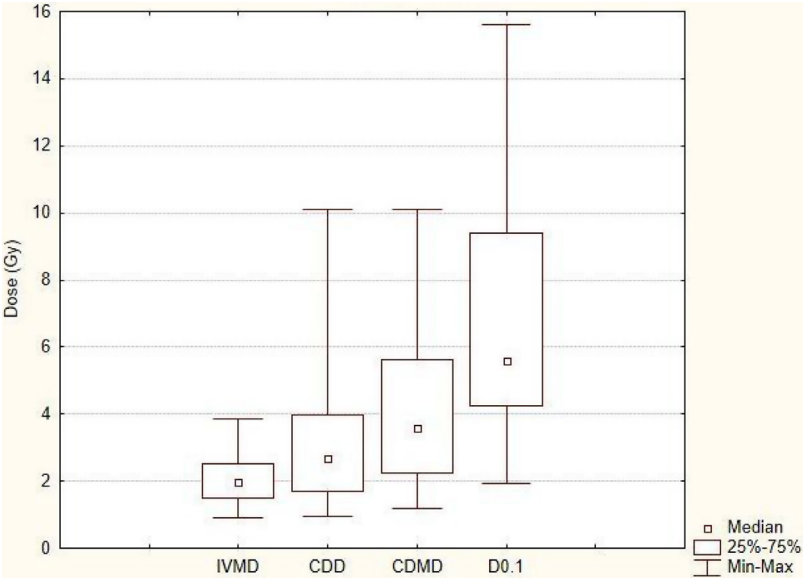

Fig. 7 – In vivo measured doses (IVMD), calculated dose of the diode where the device measured the maximal dose (CDD), calculated dose of the most irradiated diode (CDMD) and calculated volumetric maximal dose (the minimal dose of the most exposed 0.1 ccm, D0.1) of the rectum.

only available dose verification method. It this case, a general correction factor for the underestimated dose is not feasible because of the different standard deviation of the measured (IVMD) and delivered (D0.1) dose.

5. Conclusions

Under treatment conditions, the semiconductor diode does not provide reliable measuring results. The probe pushes the rectal wall closer to the high dose areas and underestimates the dose of the rectum. Higher doses are measured with a larger error, therefore, closer to the source the accuracy decreases significantly. Semiconductor probe is not recommended for in vivo dosimetry of the rectum in image-guided brachytherapy of cervical cancer.

Contributions

Georgina Fröhlich: she worked out the concept, performed the measurements in patients and did the analysis and wrote this paper.

Kinga Dóra Kovács: she performed the measurements in water.

Tibor Major: he is the head of Physics Department. He supported the study and discussed about the details.

Csaba Polgár: he is the executive medical director of National Institute of Oncology, Budapest and head of Centre of Radiotherapy. He supported the study.

Conflict of interest

This paper was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

Financial disclosure

This paper was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

Acknowledgments

This paper was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

The informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

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