IN VIVO DOSIMETRY USING A LINEAR MOSFET-ARRAY DOSIMETER TO DETERMINE THE URETHRA DOSE IN $^{125}$I PERMANENT PROSTATE IMPLANTS


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Purpose: In vivo dosimetry during brachytherapy of the prostate with $^{125}$I seeds is challenging because of the high dose gradients and low photon energies involved. We present the results of a study using metal-oxide-semiconductor field-effect transistor (MOSFET) dosimeters to evaluate the dose in the urethra after a permanent prostate implantation procedure.

Methods and Materials: Phantom measurements were made to validate the measurement technique, determine the measurement accuracy, and define action levels for clinical measurements. Patient measurements were performed with a MOSFET array in the urinary catheter immediately after the implantation procedure. A CT scan was performed, and dose values, calculated by the treatment planning system, were compared to in vivo dose values measured with MOSFET dosimeters.

Results: Corrections for temperature dependence of the MOSFET array response and photon attenuation in the catheter on the in vivo dose values are necessary. The overall uncertainty in the measurement procedure, determined in a simulation experiment, is 8.0% (1 SD). In vivo dose values were obtained for 17 patients. In the high-dose region (> 100 Gy), calculated and measured dose values agreed within 1.7% ± 10.7% (1 SD). In the low-dose region outside the prostate (< 100 Gy), larger deviations occurred.

Conclusions: MOSFET detectors are suitable for in vivo dosimetry during $^{125}$I brachytherapy of prostate cancer. An action level of ± 16% (2 SD) for detection of errors in the implantation procedure is achievable after validation of the detector system and measurement conditions. © 2009 Elsevier Inc.

In vivo dosimetry, MOSFET, Permanent prostate implant, Dose evaluation, Treatment planning system, Iodine-125.

INTRODUCTION

Brachytherapy using transperineal interstitial permanent prostate implants (TIPPB) administers a highly conformal dose to the tumor volume. However, uncertainties in seed positioning during the implantation procedure, errors in needle positioning, seed migration, or variations in seed activity may cause deviations from the prescribed dose. Several studies evaluated the dose in the prostate and organs at risk (OARs) after TIPPB, using a postimplant CT scan and the treatment planning system (TPS) to calculate the absorbed dose (1). With this method, errors in dose calculation, such as interseed attenuation, compensation for tissue inhomogeneities, and errors in seed activity, are not easy to detect (2–4). In addition, seeds with a short interseed distance are difficult to recognize on CT images. Inaccuracies in seed registration will result in imprecise dose information. In vivo dosimetry may provide useful information about the actual dose to the urethra (5). It is useful to evaluate the implantation technique, including the accuracy of the TPS, which may offer the ability to link dose distributions in OARs to clinical side effects. Nevertheless, in vivo dosimetry during brachytherapy is challenging because of the high dose gradients and the low energy of the photons emitted by the seeds.

The aim of this study was to validate the new linear 5-metal-oxide-semiconductor field-effect transistor (MOSFET) array dosimeter for dose verification after permanent $^{125}$I prostate implants to evaluate the dose in the urethra.

METHODS AND MATERIALS

$^{125}$I brachytherapy sources (Intersource$^{125}$, International Brachytherapy, Seneffe, Belgium) with a mean nominal activity of 0.6 U

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Conflict of Interest: none.
(0.5 mCi) were used. The activity of each seed in a batch was within ± 4% of the mean nominal activity provided by the manufacturer. Our clinically applied TPS (PSID 4.1, International Brachytherapy), designed for real-time dynamic ultrasound-guided radiation therapy of prostate cancer, was used for dose calculation. This system complies with the American Association of Physicists in Medicine Task Group No. 43 (TG-43) recommendations (6). Patient planning is based on the criteria that the 145-Gy isodose line covers the prostate volume, the urethra dose does not exceed 200 Gy, and the medium rectum volume exceeding 100 Gy should be < 8 cc (7).

For dose measurements, a high-sensitivity MOSFET array (Linear 5ive MOSFET Array, TN-502LA5, Best Medical Canada, Ottawa, Canada) at the high-sensitivity-bias setting was used. The array contains five MOSFET dosimeters, which are 4 mm long, 1.8 mm wide, and 1.3 mm thick, all fixated on a 46-cm flexible cable, with 2-cm inter-MOSFET spacing. The Mobile MOSFET Dose Verification System (TN-RD70W, Best Medical Canada, Ontario, Canada) was used for online dose readout on a remote PC.

**Phantom measurements**

**Angular dependence of the MOSFET-array response.** Studies performed with single dosimeters (5, 8) and with the linear array at 60Co energies (9) demonstrated a small angular dependence. To test the angular response of the linear MOSFET array for 125I sources, the detector was placed at the center of a polymethylmethacrylate (PMMA) phantom made in-house (Fig. 1a). Three strengths, each containing of three seeds, were placed 0.5, 1, and 1.5 cm from the detector to obtain higher dose-rates and more accurate measurements. The direction from the MOSFET to the top of the black epoxy bulb of the detector was defined as 0°. The angle of the detector was varied in steps of 30° from 0° to 330°. For each angle, five measurements were obtained, and the results were averaged. The result of each angle was related to the mean result of all angles.

**Calibration.** The calibration coefficient, which converts the radiation-induced voltage shift of the detector into dose, decreases with increasing energy in the keV range (10). Therefore, the energies used for the clinical measurements should be used to assess the calibration coefficient in this low energy range. To determine the calibration coefficient for each MOSFET of the linear array, 12 125I seeds were positioned circularly around the detector using a PMMA calibration phantom (8 × 8 × 15 cm) made in-house, and the MOSFET array was placed at the center (Fig. 1b). This setup was used to simulate the clinical situation, reduce measurement time, and reduce uncertainties in the position of the detector because the dose distribution in the area of the measurement is almost homogeneous. The dose rate was calculated using the American Association of Physicists in Medicine TG-43 recommendations. We used a reference distance of 1 cm and the point of interest relative to the source longitudinal axis at the reference angle of 90°. For this type of seed, the dose-rate constant is 1.01C Gy h⁻¹ U⁻¹ (11). A supplementary correction from water to the material of the calibration phantom of 11% (12) was used.

Corrections were made for source decay during the time interval between calibration and the apparent activity, using the known half-life of 125I.

Each MOSFET was placed in the plane of the seeds, five measurements were performed for each MOSFET, and the results were averaged and compared with the calculated dose values.

**Absorption of the catheter material.** The in vivo measurements were performed with the MOSFET array placed in a catheter. The TPS assumes all material surrounding the seeds is water (i.e., the influence of catheter absorption on the dose distribution is not included). To test the difference in absorption between water and the catheter material, we performed a set of phantom measurements. A PMMA phantom made in-house, similar to the calibration phantom but with a larger hole in the center of the phantom, was used. The larger hole allowed for catheter placement. A second ring containing 12 holes for seed placement was positioned at a 2-cm distance from the detector to approach clinical dose rates. A Foley catheter, a silicone two-way catheter with an outside diameter of 6 mm (18 French) and a length of 40 cm (Ref. 170605, Teleflex Medical, Mijdrecht, The Netherlands), was positioned in the center of the phantom. The MOSFET array was placed in the catheter, and 24 strands, each containing three seeds, were placed around the detector. The phantom was placed in a water tank to fill the space between the MOSFET and catheter material with water (Fig. 1c). The position of the array was determined accurately (± 0.5 mm), having MOSFET 2 positioned in the plane of the center of the strands. The MOSFET position was related to the marks on the flexible cable of the array, relative to the top of the phantom, and defined as MOSFET position 1 (MP1).

To investigate the absorption of the catheter material in case the radiation passes the catheter under an oblique angle, the MOSFET array was pulled down along the catheter with a distance of 8.8 mm (MP2), 17.6 mm (MP3), 25.1 mm (MP4), 33.9 mm (MP5), and 42.7 mm (MP6), again by using the marks on the flexible cable in relation to the top of the phantom. For each position, five measurements were performed. The results were related to an equal set of measurements in the same phantom positioned in a water tank, but with water occupying the space where the catheter material was previously. The results are presented as the ratio of the MOSFET reading attenuated by catheter material compared with the attenuation of the same layer of water.

**Temperature dependence of the MOSFET-array response.** Ramaseshan et al. (13) described the temperature response of micro-MOSFETs, demonstrating a 0.5% variation when increasing the temperature from 20 to 40°C. The temperature dependence of the new MOSFET array was not yet described. To test the variation in MOSFET array sensitivity due to temperature changes, the large-hole phantom (without the catheter material) and 12 single seeds were used. The temperature sensor was placed inside the hole close to the MOSFET array without shielding the detector from the radiation. The phantom was positioned into a water tank, and the water temperature was varied between 19 and 40°C. MOSFET 3 was positioned in the plane of the seeds. Measurement times of 10 min were used. The temperature was determined at the start and the end of the measurement, and the mean temperature was used for the results. The results were related to initial calibration conditions at room temperature (20°C).

**Total measurement uncertainty.** The reproducibility of the MOSFET detector depends on the energy of the radiation and the integrated dose measured by the MOSFET detector. Lavallée et al. (10) reported uncertainties of about 6% (1 SD) using an orthovoltage beam with a mean energy of 30 keV and dose values of about 55 Gy. During the clinical measurements, the uncertainty may be even larger because of the lower signal and positional inaccuracies of the detector. To estimate the total uncertainty, a simulation of a complete treatment was performed. A tank, containing a urinary catheter, was filled with gelatin. Needles were inserted through the holes in the wall of the phantom. We planned a needle distribution, mimicking a clinical plan, using 19 needles and 57 seeds. After the placement of the seeds, the MOSFET array was placed in the urinary catheter, and dose values were obtained (position 1). Five
Fig. 1. Phantoms used to investigate the response of the linear MOSFET array. (a) Phantom to test the angular response. Seeds were placed 0.5, 1, and 1.5 cm from the detector. The black epoxy bulb of the detector was defined as 0°, and the angle of the detector was varied in steps of 30° from 0° to 330°. (b) Phantom for calibration of the MOSFET array to convert the radiation-induced voltage shift into dose. The linear MOSFET array is inserted in the central hole, in the plane of the seeds. (c) Setup to investigate the absorption by the catheter material. The phantom (8 × 8 × 15 cm) is placed in a water tank, and a catheter is placed at the center of the phantom. The results of the five MOSFETs (M1–M5) and six MOSFET array positions (MP1–MP6) were related to an equivalent set of measurements without the catheter material. (d) Setup to test the total measurement uncertainty, presented as a frontal view (i) and a lateral view (ii) of the phantom. The marks, illustrated in the frontal view, present the holes used for seed implantation. The lateral view presents the seed distribution, the urinary catheter and the MOSFET array positions in the catheter. MOSFET = metal-oxide-semiconductor field-effect transistor.
measurements of 10 min were performed, and the results were averaged. After the measurements, the MOSFET array was pulled out over a distance of 1 cm to obtain more dose information along the catheter (position 2). Five measurements were again performed. The in vivo dose values of both positions were extrapolated to the accumulated dose values, using the half-life \( t_{1/2} \) of \(^{125}\text{I} \):

\[
D = \text{IDR} \times (t) \text{ and } (t) = \left( \frac{t_{1/2}}{\ln 2} \right)
\]

where IDR is the initial dose rate and \( t_{1/2} \) is 59.4 days. The measurement setup is shown in Fig. 1d. Figure 1d presents a frontal view of the phantom and the template. The marks illustrate the holes that were used for seed implantation. Figure 1di presents a lateral view of the phantom, showing the seed distribution, the urinary catheter in the gelatin, and the MOSFET-positions in the catheter.

After the in vivo measurements, a dummy MOSFET array with radio-opaque markers at each MOSFET detector position was placed in the catheter. The phantom was placed in a CT scanner and 1-mm slices at 1-mm intervals were acquired for both MOSFET positions 1 and 2. The CT scans were loaded into the TPS, and the measured extrapolated dose results were compared with the TPS calculated dose values.

**Patient measurements**

**In vivo** dose measurements were performed in 17 patients. Immediately after implantation, patients were transported to the recovery. A Y-connector was inserted between the catheter and the urine bag, and a sterilized high-sensitivity linear array was placed into the catheter. The end of the array was positioned at the top of the catheter. The position of the array was fixed using a rubber wedge, which also prevented urine leakage from the catheter. Measurements were performed for 1 hour, with automatic readout every 5 min. Constant dose rate was assumed during the interval because of the half-life of \(^{125}\text{I} \). After the dose measurements, the array was removed from the catheter, and the patient was transported to a CT scanner. In the scanner room, a sterilized dummy linear array was positioned to the top of the catheter and fixed with the rubber wedge. A CT scan was performed (1 mm thick at 1-mm intervals) from the bladder dome up to the perineum. The CT slices were then loaded into our TPS. In vivo dose data and calculated dose values were compared.

**RESULTS**

**Phantom measurements**

**Angular dependence of the MOSFET-array response.** The results of the measurements of the angular dependence of the detector response, related to the mean result of all angles, are shown in Fig. 2. A deviation of 3.1% (± 0.51%, 1SD) at 0° was observed, probably due to the shape of the epoxy layer that imbeds the MOSFET. The deviations at other angles were within the observed deviation at 0°. These results are comparable to those of other studies (5, 8, 9).

**Calibration.** The sensitivity of the individual MOSFETs of the MOSFET array ranged between 15.2 and 16.5 mV/cGy, resulting in an average calibration coefficient of the MOSFETs of 0.06 cGy/mV with an uncertainty of ± 6% (1 SD). These results are consistent with the values provided by the manufacturer for a random batch of MOSFET arrays.

The response of the detector was linear within 1% for dose values ranging from 0.4 to 4 cGy. For values < 0.05 cGy, the background noise exceeds the MOSFET reading, indicating that dose values < 0.05 cGy are not reliable.

**Absorption of the catheter material.** The degree of absorption by the catheter material depends on the angle of incidence of the radiation on the catheter. If the MOSFET is positioned in or very close to the plane of the seeds (MP1, MP2, and MP3), the effect of the absorption of the catheter material compared with water is almost constant. When the radiation passes the catheter obliquely, the absorption increases. The additional absorption measured by the MOSFET positioned in the catheter relative to the measurements in water is on average 9.1% for MP1, MP2, and MP3. For MP4, MP5, and MP6, the absorption is 21.8%, 24.8%, and 37.6%, respectively. A correction for catheter attenuation is therefore required. In practice, it is difficult to perform such a correction because the dose will be influenced by the number of seeds at different distances from the measuring point. We used an approach in which we linked the distance...
between the MOSFET and the seeds, and thus the angle of incidence, to the IDR. Figure 3 illustrates the deviation caused by the absorption of the catheter, plotted against IDR. For high dose rates (>5.2 cGy/h), the correction is taken to be constant (~9%), whereas for the lower dose rates (<5.2 cGy/h), the attenuation caused by the catheter was approximated by a logarithmic correction (Y = –13.835ln(IDR) + 33.1).

Temperature dependence of the MOSFET-array response. The influence of temperature on the sensitivity of the detector is illustrated in Fig. 4. Because the results are based on single measurements, a relatively large fluctuation in the data was observed. However, a linear fit through these data points demonstrated an evident deviation between MOSFET sensitivity for room temperature compared with patient temperature, showing that the MOSFET sensitivity increases with increasing temperature. The ratio of the measurements performed at room temperature compared with body temperature is 1.11 on average, and the temperature coefficient is 0.6%/°C. This means that the dose values during patient measurements will be 11% higher on average compared with the values defined during phantom measurements. A correction is therefore required. When the MOSFET-temperature is constant, a fixed correction of 11% can be applied to the in vivo dose values.

Total measurement uncertainty. The total measurement accuracy, determined during the simulation of the clinical plan (at room-temperature), corrected for catheter attenuation, can be derived from Fig. 5. The shapes of the measured and calculated curves correspond reasonably well. The observed average deviation between measured and calculated dose values is 4.9% ± 8.3% (1 SD) for MOSFET position 1 and –0.4% ± 7.6% (1 SD) for MOSFET position 2. The overall mean of both measurements is 2.3% ± 8.0% (1 SD), with the measured dose values higher than the calculated dose values.

The uncertainty in the measurements is higher in the low-dose-rate regions compared with the high-dose-rate region because of an increase in the signal-to-noise ratio of the dosimeter. For dose rates below 4.8 cGy/h, the measurement uncertainty is 9.5% (1 SD). For dose rates ≥ 4.8 cGy/h, the uncertainty is 4.8%.

Patient measurements

The position of the MOSFET array, relative to the prostate 200-Gy isodose line in a patient, is presented in Fig. 6a and 6b, showing a sagittal view and an oblique view, respectively. Figure 6b illustrates that the 200-Gy isodose line and MOSFET position do not overlap, demonstrating that the dose in the urethra does not exceed 200 Gy.

The measurements demonstrated that the mean IDR in the bladder neck, observed by MOSFET 1, was 0.7 ± 0.3 cGy/h (1 SD). With distance from the bladder toward the prostate gland, the dose rates increased and reached their maximum inside the prostatic urethra where a mean IDR of 5.9 ± 1.3 cGy/h was observed. The highest dose rates were observed for MOSFETs 3 and 4, depending on the length of the prostate. Extrapolated to the accumulated dose (D), the maximum observed dose was 197 Gy. Toward the perineum, dose rates decreased to 1.6 cGy/h, as measured by MOSFET 5.

The mean deviation between measured and calculated dose values corrected for temperature dependence of the detector response and catheter absorption is 9.2% ± 22.3% (1 SD). This large deviation is mainly due to uncertainties in the lower dose area (extrapolated dose values < 100 Gy or IDR < 4.8 cGy/h), where a mean deviation of 12.0% ± 24.7% (1 SD) was observed. In the high-dose area (accumulated dose > 100 Gy), in or close to the prostatic gland, the mean deviation was 1.7% ± 10.7% (1 SD). The global dose deviation, given as the dose relative to the highest dose value measured with a MOSFET in a particular patient, is, however, a more realistic way to express the deviations in...
this low-dose region. Thus, the mean deviation of all points was 1.6% ± 9.2% (1 SD), and for the lower dose region (≤ 100 Gy), it was 1.5% ± 7.2% (1 SD). Both corrected and uncorrected global dose deviations, relative to the maximum dose value, are presented in Fig. 7.

**DISCUSSION**

In this study we demonstrate that, to perform *in vivo* dosimetry in brachytherapy, a good validation procedure of the detector system under clinical conditions is important. If detectors used for this purpose have well-known characteristics, *in vivo* dosimetry is a good tool for quality assurance of the treatment process and a prerequisite to relate dosimetric parameters to clinical outcome. In addition to the use of *in vivo* dosimetry after TIPPB, this approach could also be used for other brachytherapy techniques, such as high dose rate brachytherapy of prostate cancer or of other cancer sites.

The linear MOSFET array is suitable for measurements after TIPPB. In this study, a high-sensitivity array was inserted into the urinary catheter. When fully inserted, one MOSFET is generally located in the bladder neck, two or three are located in the prostate, and one or two are located beneath the prostate. A mean global deviation (related to the maximum dose values) of 1.6% ± 9.2% (1 SD) between *in vivo* and calculated results was found during our *in vivo* measurements. This result is within the measurement uncertainty and is promising.

During patient measurements, the MOSFET array is located inside a catheter, and the catheter material consequently reduces the measured dose values. To compare quantitatively the calculated and measured dose values, the latter ones must be corrected for the catheter attenuation. The extent of the absorption depends on the angle of incidence of the radiation through the catheter material. We used an approach in which we linked the distance between the MOSFET and the seeds, and thus the angle of incidence, to the IDR. For the higher dose rate areas, in or close to the prostatic gland, a correction of approximately 9% is applied, whereas for the lower dose-rate areas, the correction is a logarithmic function of IDR. This correction is not related to the MOSFET response, which is dose-rate independent.

In this study, a temperature dependence of the MOSFET array response of approximately 11% was observed, when raising the temperature from 20 to 37 °C. Ramaseshan *et al.* (13) described the temperature response of the micro-MOSFET, demonstrating a 0.5% variation when increasing the temperature from 20 to 40 °C. These different observations are due to fundamental design differences between the linear-array and the micro-MOSFET dosimeter. In the MOSFET array, the five MOSFET dosimeters share a distant common MOSFET, located at the array’s connector and always at room temperature, leading to less
compensation of the threshold voltage variations of the five MOSFETs when they reach body temperature. In the case of the micro-MOSFET, the dual-MOSFET dosimeter design is implemented on a similar silicon chip, with both sensors following similar temperature variations, leading to their differential response independent of temperature (14). After the MOSFET array’s insertion inside the catheter, it is advisable to allow a short waiting period (~5 min) to stabilize the MOSFET to body temperature before proceeding with the measurements.

An extended set of phantom measurements was performed to validate the detector system under clinical conditions. For these measurements, seeds with an activity of approximately 0.6 U (0.5 mCi) were used. The low dose rates emitted by the seeds resulted in relatively long measurement times and a higher signal-to-noise ratio. Using high-activity seeds for calibration and phantom measurements will reduce measurement times and may result in smaller measurement uncertainties (5).

The total measurement uncertainty involved in this measurement method was determined by simulating the procedure in a phantom and comparing the in vivo dose measurement results with calculated dose values. The uncertainty of these measurements is ±8.0% (1 SD). Given these results, action levels for in vivo measurements of ±16% (2 SD) should be achievable. When the dose difference exceeds the action level, the cause of the deviation between the planned and measured dose distribution will be investigated, and that knowledge may be used for future implantations.

Cygler et al. (5) described the use of MOSFET detectors for dosimetric verification after TIPPB. In that study, the feasibility of micro-MOSFET detectors for quality assurance and in vivo dosimetry of the urethra was investigated, showing that MOSFET detectors are suitable for clinical dosimetry after TIPPB. The micro-MOSFET was used and moved along the urethra in 1-cm steps, because at the time of the study, a variety of MOSFETs was not yet available. This method is, however, time-consuming and introduces an uncertainty in MOSFET position. Clinical studies describing the use of a linear MOSFET array are limited (9, 15, 16). The results on angular response agree with the results of this study; however, data about catheter absorption and temperature response were not provided.

Brachytherapy is a good tool for the treatment of prostate cancer. Although it is an effective treatment option, significant complications involving the genitourinary tract may result. A consequence of exceeding the maximum tolerable urethra dose level is acute urinary morbidity (17). Other treatment complications involve radiation proctitis and the development of a rectal ulcer (18). Real-time dosimetry during the implantation procedure is a promising tool for adjusting treatment conditions and dose values in the genitourinary tract during the implantation. Real-time dosimetry offers the opportunity to make changes in needle positioning during the procedure and avoid unacceptable dose values in organs at risk because of inaccuracies in needle positioning or seed activity. Real-time dosimetry has not yet been described and is the subject of further study in our department.

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