



UNIVERSITY OF LEEDS

This is a repository copy of *Real-time in vivo dosimetry in high dose rate prostate brachytherapy*.

White Rose Research Online URL for this paper:
<http://eprints.whiterose.ac.uk/100200/>

Version: Accepted Version

Article:

Mason, J, Mamo, A, Al-Qaisieh, B et al. (2 more authors) (2016) Real-time in vivo dosimetry in high dose rate prostate brachytherapy. *Radiotherapy and Oncology*, 120 (2). pp. 333-338. ISSN 0167-8140

<https://doi.org/10.1016/j.radonc.2016.05.008>

© 2016 Elsevier Ireland Ltd. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <http://creativecommons.org/licenses/by-nc-nd/4.0/>

Reuse

Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

Real-time in-vivo dosimetry in high dose rate prostate brachytherapy

Josh Mason^a, Arielle Mamo^b, Bashar Al-Qaisieh^a, Ann M Henry^{a,c}, Peter Bownes^a,

a - Leeds Cancer Centre, Leeds, UK

b - Sir Anthony Mamo Oncology Centre, San Gwann, Malta

c - University of Leeds, UK

Corresponding author:

Josh Mason

Department of Medical Physics

St James's University Hospital

Leeds LS9 7TF

United Kingdom

44 113 20 67905

joshua.mason@nhs.net

Running title:

HDR prostate in-vivo dosimetry

Keywords:

in-vivo dosimetry; prostate brachytherapy; dose verification

Background and purpose Single fraction treatments of 15Gy or 19Gy are common in HDR prostate brachytherapy. In-vivo dosimetry (IVD) is therefore important to ensure patient safety. This study assesses clinical IVD and investigates error detection thresholds for real-time treatment monitoring.

Material and methods IVD was performed for 40 treatments planned using intra-operative trans-rectal ultrasound (TRUS) with a MOSFET inserted into an additional needle. Post-treatment TRUS images were acquired for 20 patients to assess needle movement. Monte Carlo simulations of treatment plans were performed for 10 patients to assess impact of heterogeneities. Per-needle and total plan uncertainties were estimated and retrospectively applied to the measured data as error detection thresholds.

Results The mean measured dose was -6.4% compared to prediction (range +5.1% to -15.2%). Needle movement and heterogeneities accounted for -1.8% and -1.6% of this difference respectively (mean values for the patients analysed). Total plan uncertainty ($k=2$) ranged from 11% to 17% and per needle uncertainty ($k=2$) ranged from 18% to 110% (mean 31%). One out of 40 plans and 5% of needles were outside $k=2$ error detection threshold.

Conclusions IVD showed good agreement with predicted dose within measurement uncertainties, providing reassurance in the accuracy of dose delivery. Thresholds for real-time error detection should be calculated on an individual plan/needle basis.

Introduction

Evidence of the dose-response relationship in prostate cancer [1] has led to increases in the dose per fraction delivered in high dose rate (HDR) prostate brachytherapy with up to 19 Gy prescribed to the 100% isodose in some monotherapy treatments [2]. It is therefore important to have confidence in the dose that is being delivered and there is increasing interest in performing in-vivo dosimetry (IVD) [3,4]. UK guidelines recommend that IVD is performed for most radiotherapy patients at the beginning of their treatment [5]. HDR prostate brachytherapy treatments use a single source sequentially stepping through a set of needles and so it could be possible to monitor the treatment in real-time and interrupt and correct if a significant error is detected. In this study the feasibility of this approach is investigated using clinical IVD data from 40 HDR prostate brachytherapy patients.

IVD in HDR prostate brachytherapy has been implemented by Suchowerska et al [6] using a scintillation detector in the urethral catheter and by Seymour et al [7] using a diode array inside a dummy ultrasound probe in the rectum, however these studies did not analyse measured data in terms of real-time per-needle measurements. TLDs have given good results for HDR prostate brachytherapy IVD [8-10] but do not allow a real time measurement approach. Haughey et al [11] used a metal-oxide semiconductor field effect transistor (MOSFET) linear array inside the rectum during HDR prostate brachytherapy but concluded that the approach was not suitable due to the difficulties of quantifying uncertainties in MOSFET response. IVD in permanent seed implant prostate brachytherapy has also been investigated [12-14].

Dose gradients and position uncertainties of sources and detectors result in large and variable uncertainties in brachytherapy IVD. Real-time IVD error detection cannot use a simple error threshold but requires uncertainties to be estimated for individual catheters based on treatment plan data. This was demonstrated by Kertscher et al [15] who used Monte Carlo (MC)

simulations of random source position shifts to estimate uncertainties that were applied to measurements with simulated treatment errors.

In this study we report our clinical experience of IVD using a microMOSFET (model TN-502RDM-H Best Medical, Ottawa, Canada, hereafter referred to as MOSFET) inserted into an additional needle during intra-operative trans-rectal ultrasound (TRUS) based HDR prostate brachytherapy. An uncertainty analysis is performed including MC simulations to assess the impact of heterogeneities on dose, post-treatment imaging to assess the impact of needle movement between planning and treatment delivery, evaluation of position dependent uncertainties and other MOSFET and dose calculation related uncertainties. The uncertainty analysis is used to define error detection thresholds for per-needle and total plan measurements, and these thresholds are retrospectively applied to the IVD results to assess the feasibility of real-time treatment monitoring.

Method

MOSFET calibration and commissioning

MOSFET calibration and commissioning used a 30 cm x 30 cm x 30 cm water tank with additional solid water underneath to ensure adequate scatter. The tank was fitted with two aligned template grids through which steel needles were inserted to create an accurate, rigid geometry. All measurements were performed using the same Flexitron afterloader (Elekta AB, Stockholm, Sweden) and ^{192}Ir source used in clinical treatments. For calibration, the MOSFET was placed in a central steel needle and was irradiated using 4 needles arranged at cardinal angles around the MOSFET needle, to minimize dose gradient at the MOSFET position, and with a source-MOSFET distance of 1.5 cm to minimize the energy dependence correction that would need to be applied to clinical measurements. The MOSFET sensitivity factor was determined from the ratio of the MOSFET reading to the expected dose calculated using MC simulation of the water tank setup, using the MC simulation framework described below. Three

repeated measurements of ~2Gy were taken. Calibration measurements were repeated 4-5 times through the MOSFET lifetime of 20000mV to assess fade in response with accumulated mV. Additional details on calibration are included in supplementary material.

The water tank was also used to investigate other properties of MOSFET response. A correction for energy dependence of MOSFET response was determined from measurements varying the source-MOSFET distance between 1 cm and 5 cm - additional details are included in supplementary material. Angular dependence was tested by fixing the MOSFET in a single position and irradiating from source positions at a range of polar and azimuthal angles. Linearity of response was tested by delivering doses from 0.1 - 20 Gy to the MOSFET. Temperature dependence between room temperature used for calibration and body temperature was tested by repeating calibration measurements with the water at 37 °C and allowing the MOSFET to stabilize at this temperature for 10 minutes.

Clinical measurements

IVD measurements were performed for 40 prostate cancer patients with intermediate or high risk disease treated between July 2014 and September 2015. Thirty-three patients received a single fraction boost followed by 37.5 Gy in 15 fractions of external beam to the prostate and seminal vesicles [16] and 7 patients received a single fraction monotherapy treatment [2]. Plans were prescribed to the prostate D_{90} , with 15 Gy and 19 Gy to the 100% isodose levels for boost and monotherapy treatments respectively. Needles were inserted under TRUS guidance, treatments were planned from TRUS images using the Oncentra Prostate™ treatment planning system (TPS) v4.1.3 (Elekta AB), DVH-based inverse optimisation (referred to as DVHO in Oncentra Prostate™) [17] and delivered in a single theatre session with the patient remaining in the same position with ultrasound probe in-situ for the entire procedure. Treatments were delivered using a Flexitron afterloader (Elekta AB) and stainless steel needles (interstitial bevel needle product number 083.045, Elekta AB). Needles are inserted approximately 1

cm apart around the periphery of the prostate with 2-5 needles inserted more centrally for dose coverage of the base and apex of the gland. Dwell positions were activated throughout the PTV with 2 mm spacing. Plan objectives were prostate $V_{100} > 95\%$, PTV $V_{100} > 95\%$ (PTV = prostate + 3 mm, 0 mm posteriorly). Constraints were urethra $D_{10} < 17.5$ Gy and rectum $D_{2cm^3} < 11.8$ Gy, $V_{100} = 0$ for boost [16] and urethra $D_{10} < 22$ Gy, $D_{30} < 20.8$ Gy, $V_{150} = 0$ and rectum $D_{2cm^3} < 15$ Gy, $V_{100} = 0$ for monotherapy [2].

For IVD the MOSFET was inserted into an additional needle placed below or to the side of the urethra. The central position allows the MOSFET to sample as equal as possible dose contribution from each treatment needle, and reduces the dose gradient at the MOSFET position. The MOSFET needle is inserted to depth ~1 cm caudal to the prostate base, sufficient for the MOSFET to reach mid-gland and for the needle to be clearly distinguished from treatment needles (as it protrudes ~2cm further from the template) to reduce the risk of accidental connection to the afterloader. For simplicity the centre of the MOSFET bulb is always inserted 189 mm into the (200 mm long) needle, this corresponds to the most distal needle source position and allows the MOSFET position to be reconstructed using the source positions defined in the TPS. After the treatment plan is approved and before treatment delivery, the expected MOSFET reading is determined as follows. The contribution to the dose at the MOSFET position from each individual source dwell position is exported from the TPS, along with the MOSFET and source co-ordinates. The predicted MOSFET accumulated mV reading is calculated by multiplying each individual dwell position's planned dose contribution to the MOSFET by the MOSFET mV/Gy sensitivity factor and a correction for the MOSFET's energy dependent response. An example patient case is included in supplementary material. Per-needle and total plan readings are calculated by summing the individual dwell position contributions.

The MOSFET is inserted after the treatment needles have been connected to the afterloader, ~10 minutes before treatment starts. A mark on the MOSFET cable 189 mm back from the MOSFET is lined up to the edge of the needle, to ensure correct insertion depth. The MOSFET reader takes a reading every 20 s and is monitored remotely by camera during treatment. The Flexitron takes > 20 s between each needle delivery allowing the per needle mV reading to be determined.

Monte Carlo simulations

MC simulations were performed for 10 patient plans to determine the impact of heterogeneities on dose at the MOSFET position. DICOM treatment plan data were exported from the TPS into an MC simulation framework that has previously been described [18] using the Flexitron source modeled and benchmarked using data from AAPM report 229 [19] and using MCNPX v2.5.0 [20]. The simulation model included ANSI 303/304 steel needles modeled with density 8.02 gcm^{-3} and prostate tissue with density 1.04 gcm^{-3} and composition as recommended in TG-186 (AAPM Task Group No. 186 Report) [21] Table III. Dose at the MOSFET position was calculated using a 1 mm diameter spherical water cell (MCNPX F6 tally) and 200-400 million histories (depending on the implant size) were simulated to achieve statistical uncertainty in the tally cell of ~0.5%.

Analysis of post-treatment imaging

To assess the impact of needle movement between planning TRUS image acquisition and treatment (typically ~1 hour), for 20 of the patients, a TRUS volume was acquired immediately after completion of treatment. The needles were reconstructed in the post-treatment images, the dose at the MOSFET position was recalculated using the adjusted needle positions and compared to the original planned dose.

Uncertainty analysis

An uncertainty analysis was performed to estimate per-needle and total plan error detection thresholds. Table 1 lists the uncertainty components included in the analysis. MOSFET calibration uncertainty was estimated from the standard error of repeated measurements. Energy dependence correction uncertainty was estimated as the standard error of the actual corrections applied across all patients. An uncertainty of 3% for anisotropic response was included in the per-needle uncertainty as this was the level of repeat measurement uncertainty in the commissioning anisotropy measurements. For total plan measurements this was not included as the central MOSFET measurement position should ensure any small angular variations in response average out. Source calibration and TPS dose calculation uncertainties were taken from published data [22]. MOSFET reproducibility uncertainty was calculated from the predicted reading for each needle/plan using data on the standard error of sets of repeated measurements at different dose levels, described in supplementary data.

Position uncertainty was calculated for each needle/plan based on the source positions and predicted dose contributions as follows. A source-MOSFET distance uncertainty threshold of 1mm was used as a study by Milickovic et al [23] found needle shifts of 1 mm on average between planning and treatment in TRUS based HDR prostate brachytherapy, and that this level of shift did not have clinically significant impact on plan dosimetry. For each source position the impact of ± 1 mm shifts in the source-MOSFET distance was estimated using inverse square law. The per-needle and total plan position uncertainties were then estimated by taking a weighted average of the uncertainty for each source position (weighted by the dose per source position as a proportion of the total dose). For the total plan uncertainty, this weighted average was divided by the square root of the number of needles in the plan as the uncertainties associated with individual needles are not independent, for example if the MOSFET moves closer to one needle it will move further from another. An example position uncertainty calculation is included in supplementary data. All uncertainty components were combined in quadrature and the result multiplied by 2 to give the $k=2$ value.

Evaluation of error detection thresholds

The measured clinical data was retrospectively compared to the calculated uncertainty values to evaluate the use of error detection thresholds for real-time decision making. Firstly the mean corrections determined from the MC simulation and post-treatment imaging investigations described above were applied as a fixed percentage correction across all per-needle and total plan measurements. Measurements were considered to exceed the threshold if the percentage difference between measured and predicted values exceeded the $k=2$ uncertainty for the needle or plan.

Results

MOSFET calibration and commissioning

MOSFET sensitivity factors used in the clinical measurements ranged from 89.7 mV/Gy - 96.1 mV/Gy. Sensitivity factors were found on average to decrease by 0.24 mV/Gy for every 1000 accumulated mV. Energy dependence correction measurements showed the MOSFETs to over-respond by 2.6% cm^{-1} increase in source-MOSFET distance. The MOSFET response was linear up to 20 Gy. Angular variation of MOSFET response was less than the repeat measurement uncertainty of 3%. Calibration measurements did not vary between room and body temperature. More details on MOSFET calibration and commissioning are included in supplementary data.

Clinical measurements

For the 40 patient treatments, mean (and range) of prostate D_{90} values were 17.1 Gy (16.2 Gy - 17.6 Gy) for boost treatments and 21.1 Gy (20.8 Gy - 21.4 Gy) for monotherapy treatments. Mean (and range) of prostate volume and number of treatment needles was 35.6 cm^3 (16.7 cm^3 - 55.7 cm^3) and 15.8 (10 - 19) respectively. Mean (and range) of dose at the MOSFET position was 17.7 Gy (15.2 Gy - 20.7 Gy) for boost treatments and 21.8 Gy (20.1 Gy - 26.4 Gy) for monotherapy treatments.

Considering mean values for the 40 patients, the total plan measured MOSFET reading was 6.4% lower than predicted (range +5.8% to -14.6%). Figure 1 shows all patient measurements in terms of absolute measured dose. Figure 2a shows one example measurement curve. Mean per-needle reading for the 40 patients was also 6.4% lower than prediction with standard deviation 17.3% and range -129% to +185%. The mean total plan energy dependence correction applied was 1.6% (range 0.5% - 3.2%). The mean per-needle energy dependence correction applied was 1.3% (range -2.3% - 4.9%).

Monte Carlo simulations

MC simulations showed that the dose at the MOSFET position was on average -1.6% compared to the dose predicted by the TPS (mean for 10 patients, range -1.0% to -2.0%).

Analysis of post-treatment imaging

Post-treatment TRUS images showed either minimal difference in needle positions or some posterior movement of the more posterior needles. In all cases needle displacements were <2 mm. In the post treatment reconstructions on average the dose at the MOSFET position was -1.8% compared to the original treatment plan (mean for 20 patients, range +0.9% to -5.3%).

Evaluation of error detection thresholds

Figure 2b shows an example of the predicted and measured readings compared to uncertainty thresholds. One out of 40 plans (2.5%) and 28 out of 628 (4.5%) needles exceeded the $k=2$ error detection threshold in the retrospective analysis. The plan outside it's threshold measured -12.1% compared to a threshold of $\pm 11.8\%$. Post-treatment images for this patient showed dose reduction at the MOSFET position of 3.8%. The 28 needles outside the thresholds were in 16 patient plans and tended to have low predicted readings with mean 59.0 mV (range 5.1 mV - 153.2 mV)

compared to mean for all needles 106.5 mV and/or low absolute differences with 19/28 having measurement difference less than 20mV (~ 0.2 Gy) and 27/28 having measurement difference less than 50mV (~ 0.5 Gy). Individual cases for needles with >20 mV measurement difference and outside the uncertainty threshold were investigated retrospectively and in the majority of cases were likely to be due to needle reconstruction errors, although it is not possible to absolutely confirm this as is difficult to definitively identify a needle location in retrospective analysis of TRUS images. Four needles had a measurement difference of >100 mV (~ 1 Gy) from prediction yet were within the error threshold due to close proximity with the MOSFET.

Discussion

This study has investigated IVD in HDR prostate brachytherapy in a retrospective analysis of clinical measured data for 40 patients. Overall the IVD results give confidence in the accuracy of dose delivery. After applying the corrections from the MC simulation and post-treatment imaging investigations, the mean difference between measured and predicted total plan reading is -3.0% and the largest difference is -11.2%. Comparable measurements were made by Suchowska et al [6] using a scintillation detector in the urethral catheter for CT planned treatments and achieved maximum deviation from planned dose of -9% for 10 patients (mean deviation was not stated but from the data presented can be calculated to be -3.3%) and also by Seymour et al [7] using a diode array in the rectum for 28 patients finding 95% of measurements agreeing with predicted dose within $\pm 20\%$. In this study the MOSFET was placed in an additional needle which gives a stable position that can be accurately reconstructed. However a limitation is that for very small prostates it can be difficult to find a suitable empty template position that does not risk the MOSFET needle perforating the urethra and on approximately five occasions over the period of this study we did not perform IVD for this reason.

MC simulations showed that steel needles reduced dose at the MOSFET position by 1.6% which is comparable to a study by Gaudreault et al [24] which found dose reduction of 1.3%. Needle movement in TRUS planning was investigated by Milickovic et al [23] who found an average reduction in urethra $D_{0.1\text{cm}^3}$ of 2.1% compared to a point dose reduction at the MOSFET position (generally close to the urethra) of 1.8% in this study. MOSFET measurements were ~3% low after these corrections had been applied. This apparently systematic difference could be due to an as yet undetected error in the MOSFET commissioning/calibration process or limitations in ultrasound reconstruction accuracy - the probe remains in the rectum during treatment but there could be differences in implant position compared to image acquisition where the probe is being moved through the rectum and compressing the prostate.

This study has investigated the feasibility of real-time IVD to detect errors during treatment. This requires estimation of measurement uncertainties on a per-needle basis. Per-needle position uncertainty dominates and it is important to avoid falsely detecting an error for needles that are close to the MOSFET so tend to contribute a large proportion of the total dose, and only require a small positional shift to generate a large change in the MOSFET reading. It can be hard to position the MOSFET needle in a low dose gradient region, particularly for small prostates, and the MOSFET reading can be dominated by the contribution of a single needle with large associated uncertainties (in the worst case in this study ~1/3 of the total plan dose to the MOSFET was contributed from a single needle).

Position uncertainty was estimated using an inverse square approximation for a position tolerance of 1mm. This method is simple to implement in a spreadsheet and could easily be calculated between plan approval and treatment delivery. Kertscher et al [15] used random position error simulations to estimate position uncertainties in a statistical manner and found $k=1$ position uncertainties up to 15.9% compared to 55.1% in this study, however the closest source-detector position was 6 mm compared to

2.7 mm in this study. Although large position uncertainties were derived for some needles in this study these were calculated using position shifts of 1mm which would not be clinically significant [23]. For 91% of the needles analysed, the position uncertainty was $< 20\%$.

In this study ~5% of needle measurements exceeded the error threshold which is appropriate for a $k=2$ uncertainty level. The majority of these needles had low absolute mV predicted readings, therefore the uncertainty calculation could be under-estimating uncertainty for low readings. To reduce false positive errors a real-time monitoring method should also look at the absolute effect of any measurement difference as many of the needle measurements that exceeded the error threshold in percentage terms were only contributing a small amount to the total MOSFET dose.

A limitation of this IVD technique is the single point of measurement, which means that some errors could go undetected, and makes it difficult to assess the overall dosimetric impact of errors that are detected. A connector swap error for two needles that are the same distance from the MOSFET will not be detected but could be clinically significant - for example if a heavily weighted peripheral needle and lowly weighted needle close to the urethra were swapped causing urethral overdose and prostate underdose. It may be possible to improve detection by analysing measurements for each 20s reading provided by the MOSFET, rather than just per needle dose, or by using a device that provides more frequent or continuous measurements. The MOSFETs have limited lifetime and require significant commissioning work and individual, repeated calibrations but are relatively inexpensive and performing the IVD does not add significant time to our planning procedure.

MOSFET IVD is a useful tool for dose delivery verification and suitable for routine clinical use. It can be used for real-time treatment monitoring as long as the limitations of the measurement technique and uncertainties are understood.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

References

- [1] Dearnaley DP, Jovic G, Syndikus I, et al. Escalated-dose versus control-dose conformal radiotherapy in prostate cancer: long-term results from the MRC RT01 randomised controlled trial. *Lancet Oncology* 2014;15(4):464-73
- [2] Hoskin P, Rojas A, Ostler P, et al. High-dose-rate brachytherapy alone given as two or one fraction to patients for locally advanced prostate cancer: Acute toxicity. *Radiotherapy and Oncology* 2014;110(2):268-71.
- [3] Kertzscher G, Rosenfeld A, Beddar S, Tanderup K, Cygler J. In vivo dosimetry: trends and prospects for brachytherapy. *The British journal of radiology* 2014;87:20140206.
- [4] Tanderup K, Beddar S, Andersen CE, Kertzscher G, Cygler JE. In vivo dosimetry in brachytherapy. *Medical physics* 2013;40:070902.
- [5] Donaldson S. Towards safer radiotherapy. British Institute of Radiology, Institute of Physics and Engineering in Medicine, National Patient Safety Agency, Society and College of Radiographers, The Royal College of Radiologists, London 2007.
- [6] Suchowerska N, Jackson M, Lambert J, Yin YB, Hruby G, McKenzie DR. Clinical trials of a urethral dose measurement system in brachytherapy using scintillation detectors. *International Journal of Radiation Oncology* Biology* Physics* 2011;79:609-615.
- [7] Seymour EL, Downes SJ, Fogarty GB, Izard MA, Metcalfe P. In vivo real-time dosimetric verification in high dose rate prostate brachytherapy. *Medical physics* 2011;38:4785-4794.
- [8] Anagnostopoulos G, Baltas D, Geretschlaeger A, et al. In vivo thermoluminescence dosimetry dose verification of transperineal ¹⁹²Ir high-dose-rate brachytherapy using CT-based planning for the treatment of prostate cancer. *International Journal of Radiation Oncology* Biology* Physics* 2003;57:1183-1191.
- [9] Brezovich IA, Duan J, Pareek PN, Fiveash J, Ezekiel M. In vivo urethral dose measurements: a method to verify high dose rate prostate treatments. *Medical Physics* 2000;27:2297.
- [10] Toye W, Das R, Kron T, Franich R, Johnston P, Duchesne G. An in vivo investigative protocol for HDR prostate brachytherapy using urethral and rectal thermoluminescence dosimetry. *Radiotherapy and oncology* 2009;91:243-248.
- [11] Haughey A, Coalter G, Mugabe K. Evaluation of linear array MOSFET detectors for in vivo dosimetry to measure rectal dose in HDR brachytherapy. *Australasian Physical & Engineering Science in Medicine* 2011;34:361–366.
- [12] Bloemen-van Gurp EJ, Haanstra BKC, Murrer LHP, et al. In Vivo Dosimetry With a Linear MOSFET Array to Evaluate the Urethra

- Dose During Permanent Implant Brachytherapy Using Iodine-125. *International Journal of Radiation Oncology* Biology* Physics* 2009;75:1266-1272.
- [13] Cherpak AJ, Cygler JE, Choan E Perry G. Real-time measurement of urethral dose and position during permanent seed implantation for prostate brachytherapy. *Brachytherapy* 2014;13:169-177.
- [14] Cygler JE, Saoudi A, Perry G Morash C. Feasibility study of using MOSFET detectors for in vivo dosimetry during permanent low-dose-rate prostate implants. *Radiotherapy and oncology* 2006;80:296-301.
- [15] Kertzscher G, Andersen CE, Siebert FA, Nielsen SK, Lindegaard JC Tanderup K. Identifying afterloading PDR and HDR brachytherapy errors using real-time fiber-coupled Al₂O₃:C dosimetry and a novel statistical error decision criterion. *Radiotherapy and oncology* 2011;100:456–462.
- [16] Morton G, Loblaw A, Cheung P, et al. Is single fraction 15Gy the preferred high dose-rate brachytherapy boost dose for prostate cancer? *Radiotherapy and oncology* 2011;100:463-467.
- [17] Oncentra Prostate Reference Manual 190.037ENG-05: Nucletron.
- [18] Mason J, Al-Qaisieh B, Bownes P, Thwaites D Henry A. Dosimetry modeling for focal high-dose-rate prostate brachytherapy. *Brachytherapy* 2014;13(6):611-7.
- [19] Perez-Calatayud J, Ballester F, Das RK, et al. Dose calculation for photon-emitting brachytherapy sources with average energy higher than 50 keV: Report of the AAPM and ESTRO. *Medical Physics* 2012;39:2904.
- [20] Pelowitz DB. MCNPX User's Manual Version 2.5.0. Los Alamos National Laboratory Report 2005;LA-CP-05–0369.
- [21] Beaulieu L, Tedgren ÅC, Carrier J-F, et al. Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: Current status and recommendations for clinical implementation. *Medical Physics* 2012;39:6208-6236.
- [22] Kirisits C, Rivard MJ, Baltas D, et al. Review of clinical brachytherapy uncertainties: Analysis guidelines of GEC-ESTRO and the AAPM. *Radiotherapy and Oncology* 2014;110:199-212.
- [23] Milickovic N, Mavroidis P, Tselis N, et al. 4D analysis of influence of patient movement and anatomy alteration on the quality of 3D U/S-based prostate HDR brachytherapy treatment delivery. *Medical Physics* 2011;38:4982
- [24] Gaudreault M, Reniers B, Landry G, Verhaegen F Beaulieu L. Dose perturbation due to catheter materials in high-dose-rate interstitial 192 Ir brachytherapy. *Brachytherapy* 2014;13:627-631.

Table 1 Results of the uncertainty analysis. For variable uncertainty components the values shown are the mean with the minimum and maximum values in parentheses.

Description	Type	Per needle uncertainty	Total plan uncertainty
MOSFET calibration (k=1)	A	2.7 %	2.7 %
Energy correction (k=1)	A	1.7 %	0.3 %
Angular dependence (k=1)	A	3 %	0 %
Source calibration (k=1)*	A	2 %	2 %
TPS dose calculation (k=1)*	B	3 %	3 %
Position uncertainty (k=1)	B	13.0% (6.1% - 55.1%)	4.1% (2.7% - 7.2%)
MOSFET reproducibility (k=1)	A	3.4% (0.8% - 47%)	0.4% (0.3% - 0.5%)
Mean total uncertainty (k=2)		31.9 % (18.3 % - 111 %)	12.3 % (10.6 % - 17.0 %)

* Taken from Kirisits et al [21]

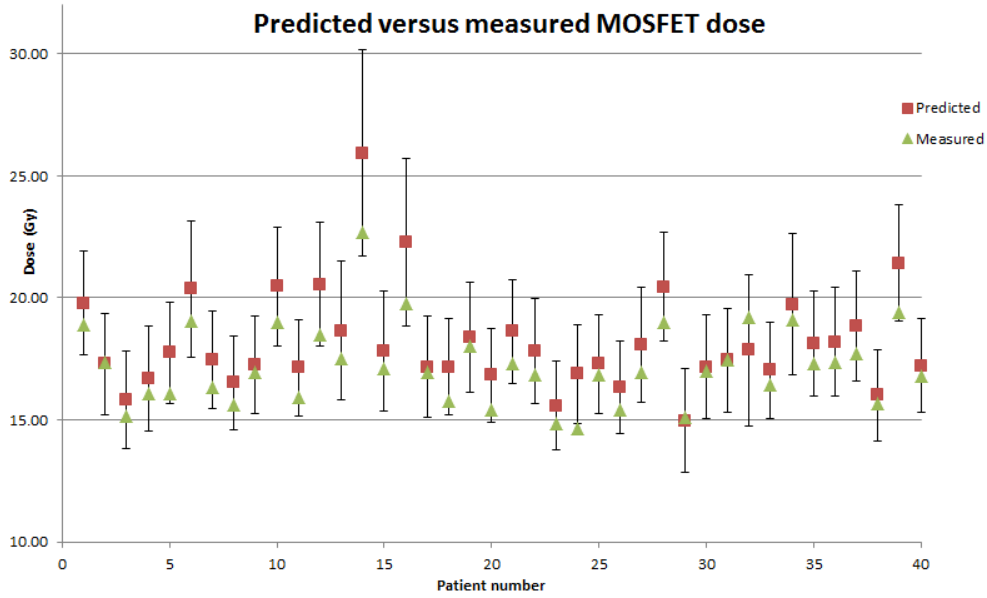


Figure 1 Predicted versus measured dose at the MOSFET position for the 40 HDR prostate brachytherapy patient treatments in this study. The error bars show the $k=2$ uncertainty for the predicted dose.

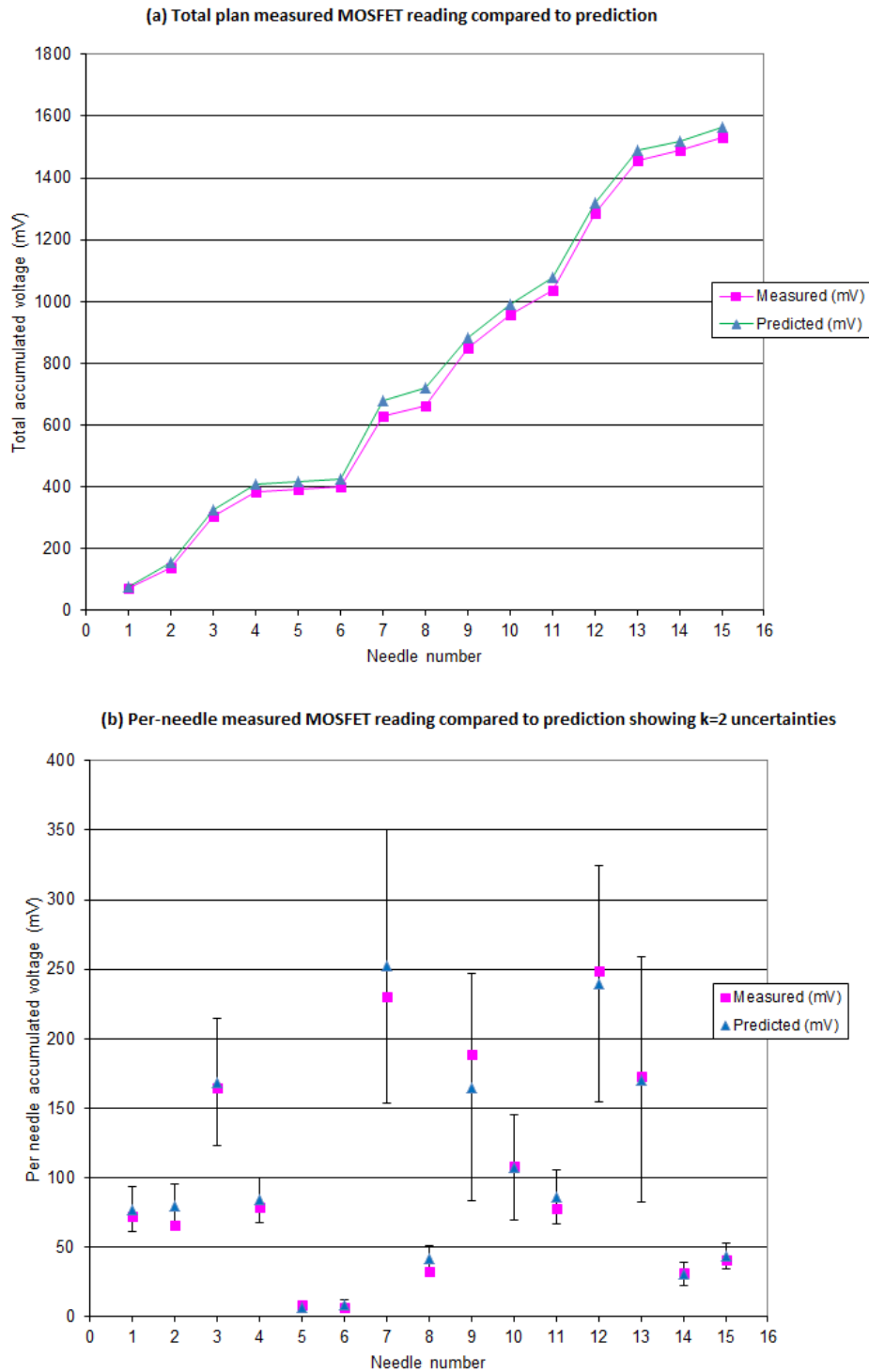
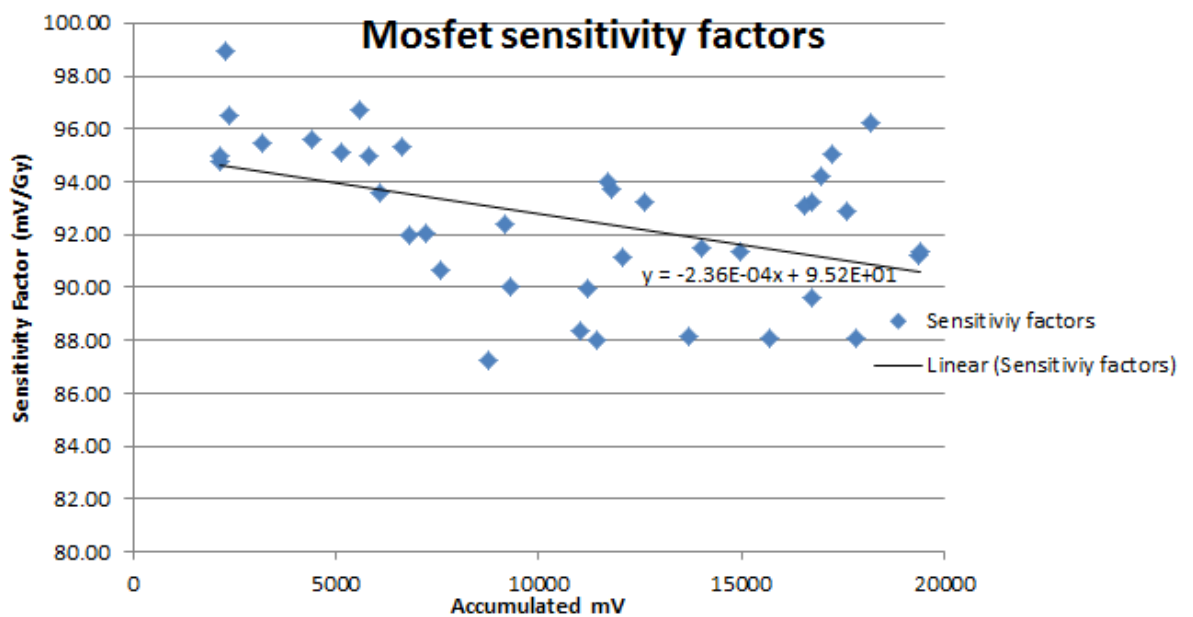


Figure 2 Measurement results for one patient (a) total accumulated MOSFET reading as the treatment is delivered (b) per needle MOSFET reading with error bars showing the $k=2$ uncertainty calculated for the predicted needle reading.

Fade in MOSFET sensitivity factor

Calibration measurements were repeated 4-5 times through the MOSFET lifetime of 20000mV to assess fade in response with accumulated mV. Early experience showed that the MOSFET sensitivity factor decreases rapidly in the initial period of use. Therefore it was decided to pre-irradiate the MOSFETs to an accumulated mV of 2000 mV to improve the stability of the sensitivity factor. Eight MOSFETs were used in the study, and the sensitivity factor was found on average to decrease by 0.24 mV/Gy for every 1000 accumulated mV once the initial 2000 mV pre-irradiation had been completed. The measured MOSFET sensitivity factors are shown in Suppl Figure 1.



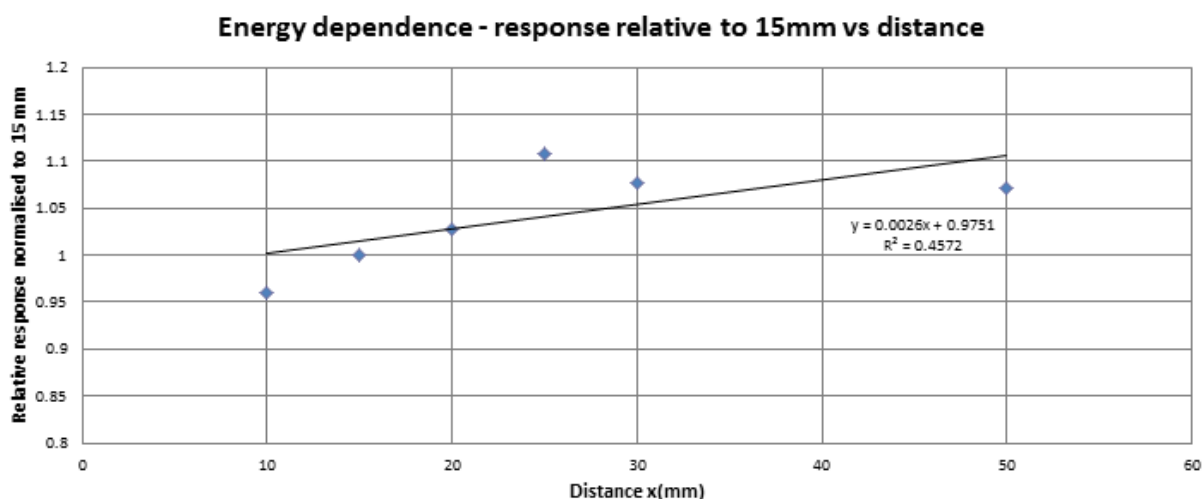
Suppl Figure 1 MOSFET sensitivity factors from all MOSFET calibrations

MOSFET energy dependence

The MOSFET energy dependent response correction was determined from water tank measurements as described above, but varying the source-MOSFET distance in the range 1 - 5 cm. For distances 1 - 3 cm the MOSFET was irradiated using 4 needles arranged at cardinal angles around the MOSFET needle, to minimize dose gradient at the MOSFET position,

for greater distances this was not possible due to the size of the template so a single source needle was used.

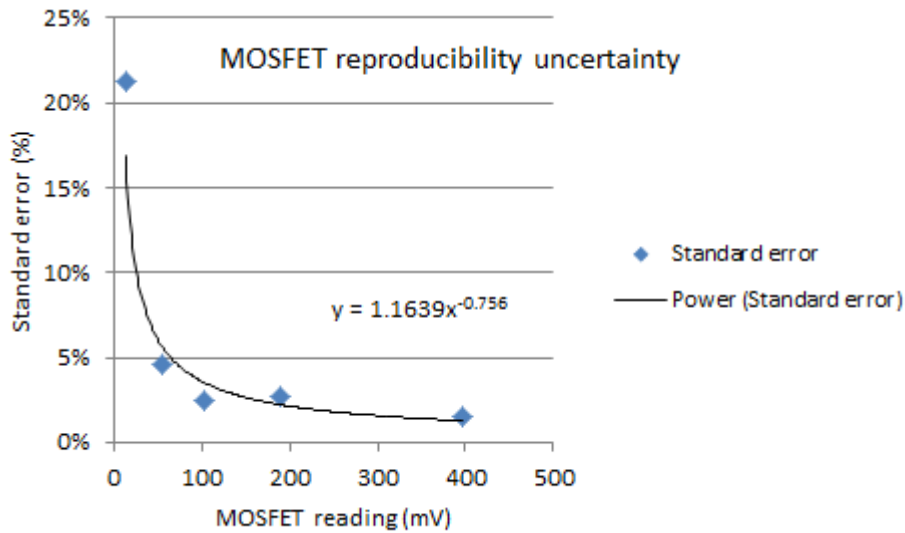
The ratio of MOSFET measurement to the measurement predicted from the MOSFET sensitivity factor using the dose calculated by the TPS was used to determine the MOSFET response relative to the calibration distance of 1.5 cm. A linear fit of response versus distance was used to determine the energy dependence correction. Suppl Figure 2 shows the results. Based on this a $2.6\% \text{ cm}^{-1}$ correction was applied to MOSFET predicted readings to correct for the energy dependence.



Suppl Figure 2 Variation of response relative to response at 15mm due to MOSFET energy dependence

MOSFET reproducibility uncertainty

Measurement reproducibility was tested by calculating the standard error of 5 repeat measurements at dose levels of approximately 0.1 Gy, 0.5 Gy, 1 Gy, 2 Gy and 4Gy. A power curve fit was applied to the results (shown in Suppl Figure 3) and the percentage reproducibility uncertainty was found to be $116.4(R)^{-0.756}$ where R is the reading in mV.



Suppl Figure 3 Standard error in repeated MOSFET measurements against size of reading.

Simple example of position uncertainty calculation

Suppose the MOSFET is at co-ordinate (0,0,0) and there are two catheters with the source positions and dose contributions shown in Suppl Table 1. For each individual source position, the position uncertainty is estimated by taking the average of the inverse square law correction for $r \pm 1$ mm (for example if $r=10$ mm then the uncertainty is the mean of $((11/10)^2 - 1)$ and $((10/9)^2 - 1)$). To estimate the position uncertainty per-needle, each source position uncertainty is weighted by the dose contribution for that source position as a proportion of the total for the needle, and the sum of the weighted source position contributions gives the per-needle uncertainty.

The position uncertainty for the total plan dose is estimated using the same method, except that the position uncertainty from each source is weighted by the dose contribution for that source position as a proportion of the total plan dose. The position uncertainty for the plan is the sum of the weighted source position contributions divided by the square root of the number of needles in the plan.

Suppl Table 1 Position uncertainty calculation example. (x,y,z) are the source position co-ordinates and r is the distance from the source to the MOSFET. The MOSFET is at (0,0,0).

Needle	x	y	z	r	Dose	Position uncertainty	Position uncertainty (weighted per needle)	Position uncertainty (weighted per plan)
1	10	0	5	11.18	1	0.196	0.065	0.022
1	10	0	0	10.00	0.5	0.222	0.037	0.012
1	10	0	-5	11.18	0.5	0.196	0.033	0.011
1	10	0	-10	14.14	1	0.152	0.051	0.017
Total for needle 1							0.186	
2	-20	10	5	22.91	1	0.091	0.015	0.010
2	-20	10	0	22.36	2	0.094	0.031	0.021
2	-20	10	-5	22.91	2	0.091	0.030	0.020
2	-20	10	-10	24.49	1	0.085	0.014	0.009
Total for needle 2							0.091	

