A prospective study on pain score with transperineal prostatic gold seed fiducial implantation under local anesthetic alone

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Abstract

Background: The purpose of this study was to monitor patient pain score with transperineal prostatic gold seed implantation in the absence of conscious sedation.

Methods: All patients who were scheduled for image-guided external beam radiation (IGRT) and referred for gold seed fiducials were eligible to participate. Gold seed implants were performed by two radiation oncologists between December 2007 and April 2008. Patients received only local and deep anesthetic. No patients had prophylactic IV cannulation for the procedure. Three gold seeds were inserted transperineally into the prostate. A visual analogue scale from 0 to 10 was used to assess the pain at baseline, local and deep anesthetic infiltration, with each seed drop, and after the completion of the procedure.

Results: A total of 30 patients were accrued to this study. The highest recorded increase in pain score was at the time point of deep local anesthesia, at which the mean pain score was 3.8. The mean pain scores at each seed drop were 0.8 (standard deviation [SD]=1.24), 1 (SD=1.26), and 0.5 (SD=0.90), respectively. All gold seed insertion procedures were well-tolerated, with no patients having significant pain post-procedure, and no significant procedural complications. There were only slight increases in dysuria, urinary frequency, constipation, urinary retention and flatulence in 7 patients – none of which required intervention.

Interpretation: Transperineal ultrasound-guided gold seed implantation without conscious sedation is well-tolerated and associated with a low complication rate. It is a convenient outpatient procedure obviating the need for resource intensive postoperative monitoring.

Introduction

Modern prostate radiotherapy is trending towards higher biological doses.[1-4] There is a greater need for better accuracy in radiation treatment delivery if toxicities are not to increase. For patients undergoing image-guided external beam prostate radiotherapy (IGRT), gold seed fiducial implantation in the prostate is common. These gold seeds are usually small (typically about 1 × 3 mm) and are chemically inert.

Being radio-opaque, gold seeds are easily identified on kilovoltage and megavoltage x-rays. This allows for daily online imaging and position adjustment before treatment. Daily online imaging based on fiducials reduces systematic and random errors, and is superior to offline imaging based on bony anatomy.[5-9] As a result, studies have established that with the use of fiducials, clinical target volume and planning target volume margins can be reduced, allowing for more sparing of normal tissues without geographical miss.[9,10]

The Odette Cancer Centre (OCC) has been using fiducials for prostate radiotherapy since 2001. Initially, conscious sedation with intravenous midazolam and fentanyl was administered to all patients prior to fiducial implantation. This required the patient to remain at the OCC for about 1 hour after the procedure for monitoring in the recovery room before discharge. Furthermore, patients were not permitted to drive themselves home. In 2007, a shift in practice was made to reduce patient inconvenience and improve safety by omitting the conscious sedation. The purpose of this study was to monitor patient pain score without conscious sedation with the change of practice. Our secondary objective was to see if simple preoperative parameters had an influence in the pain experienced with the procedure.

Methods

All patients who were scheduled for IGRT at the OCC and referred for gold seed fiducials were eligible to participate in the study. Informed consent was obtained. Where relevant and safe to do so, patients were asked to withhold their aspirin or anticoagulants for 7 days prior to the procedure. They were also given a sodium biphosphonate enema to be used the morning of the procedure to ensure adequate bowel preparation. The patient also commenced oral antibiotics the night before the procedure. Implants for this study were per-

formed by two radiation oncologists in a dedicated treatment room (high dose rate [HDR] suite) with anesthetic backup.

No patients had prophylactic intravenous cannulation for the procedure. After appropriate bowel preparation, the patient was brought into the HDR suite and placed in a dorsal lithotomy position with legs supported, abducted and flexed. Each patient's perineum was prepped with poviodine and scrotal contents elevated with a sterile towel. At this time, 10 mL of 1% lidocaine hydrochloride with adrenaline (1:100 000) was infiltrated into the perineal dermis and subcutaneous tissues (defined as superficial anesthesia for this study). A further 10 mL was directed around the bilateral posterolateral periapical region of the prostate under rigid transrectal ultrasound (TRUS) guidance. Following this, a further 5 mL of plain 1% xylocaine was infiltrated directly into the prostate gland (the periprostatic and intraprostatic infiltration is defined as deep anesthesia for this study). Prostate volume was then measured and 3 gold seeds (Best Medical International, Springfield, VA) were inserted transperineally into the prostate under TRUS guidance in a way to ensure appropriate triangulation (Fig. 1). Hemostatsis was controlled with direct pressure. Patients were discharged with prophylactic antibiotic for another 2 days once they were able to pass urine and walk without difficulty. As opposed to those patients who had conscious sedation, the patients in this study were allowed to drive home themselves.

Baseline characteristics were collected (Table 1). Specifically, patients were also asked if they were on any pain modifying medications, including simple analgesia (such as aspirin, acetaminophen and non-steriodal anti-inflammatory) in the week leading up to the implantation day. A visual analogue scale (VAS)[11] from 0 to 10 was used to assess the pain at baseline, with each seed drop, and after the completion of the procedure. Assessment was done by a radiation therapist or nurse who normally assists with the procedure. An intraoperative pain score was also collected during the procedure, rather than postoperatively, to avoid problem with recall bias. Patient records were also checked, retrospectively, for any recorded complications leading up to their planning computed tomography (CT) and start of radiotherapy.

The duration of the procedure was timed from the start of perineal sterilization with poviodine to the withdrawal of the last needle from the seed drop.

We obtained research ethics board approval from Sunnybrook Health Sciences Centre and a sample size of 30 was planned. The sample size was chosen based on convenience and as such no formal sample size calculation was conducted. Consecutive patients who had been accrued to clinical trials that required gold seed fiducial marker insertion were approached for this study at the time of gold seed insertion. All patients consented; therefore, no screening logs were used during patient accrual. It was felt that a comparative group of patients with IV sedation may not be a fair comparison as patients in the sedated group may be too drowsy to give a reliable pain score. Therefore, such a comparison was not carried out.

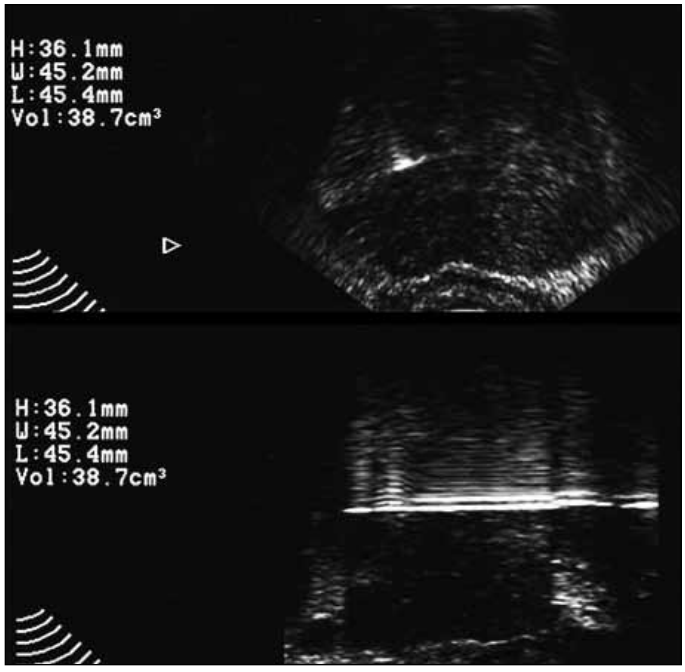

Fig 1. Axial and sagittal ultrasound view of seed placement for Patient no. 19.

During the study, there was a variation in the number of time points where pain score was collected. The first 8 patients did not have pain score recorded for superficial and deep local anesthesia. These additional time points were included subsequently when it was recognized that, although the procedure was relatively pain free with each seed drop and reflected well-established analgesia, the time points where pain score may actually be higher were being missed, specifically at the time of local anesthetic infiltration.

Results

The study was carried out from December 2007 to April 2008. A total of 31 patients were enrolled. One patient did not have pain score collected for 2 of the 3 gold seed drops inserted and was excluded from this analysis. His score for the second gold seed placement was 5. The remaining 30 patients formed the basis of this analysis.

The median age of patients accrued to this study was 71 (range: 51-81) and median prostate-specific antigen level was 9.7 ng/mL (range: 3.7-58). About a third (37%) of patients were low-risk patients and the remaining two thirds were high-risk patients (63%) (there were two hypofractionation research protocols requiring gold seed fiducial marker implantation at the time of this study).[12-13] Seventeen percent of patients were on pain-modifying medications in the week prior to the procedure. One patient was on methocarbamol-acetaminophen combination for back pain. Two patients

Table 1. Patient baseline information

Parameter	Value
Median age (range)	71 (51-81)
Median PSA (range)	9.7 (3.67-58)
Median IPSS (range)	6 (0-16)
Median prostate volume (range)	28.25 (12.7-74.5)
Gleason score (%)	
6	11 (37%)
7	6 (20%)
8	5 (17%)
9	8 (27%)
Clinical T stage (%)	
1c	14 (47%)
2a	9 (30%)
2b	1 (3%)
2c	1 (3%)
3a	5 (17%)
On pain modifiers (%)	4 (17%)
Not on any pain modifiers (%)	20 (83%)

PSA: prostate-specific antigen; IPSS: International Prostate Symptom Score.

were on non-steroidal anti-inflammatories and one was on aspirin until 4 days prior to the procedure despite being instructed to stop aspirin a week earlier.

The mean change in score from baseline at each time point is shown in Fig. 2. The highest recorded increase in pain score was at the time point of deep local anesthesia at which the mean pain score was 3.8. The lowest recorded increase in pain score was at the time point of the third gold seed insertion. Only one patient had a baseline pain score of 1 due to recent prostatitis. He previously had a course of intravenous erythromycin and although the pain score remained at 1 at the completion of his procedure, he scored it as 0 for seed 2 and 3 drop. Interestingly, one patient who admitted to being extremely anxious actually scored only 2 and 3 for the infiltration and 0 for the rest of the procedure.

All gold seed insertion procedures were uncomplicated and well-tolerated, with no patients having significant pain post-procedure. A clinically significant change in pain was defined as an increase of two or more points on the 11-point VAS scale. No significant procedural complications occurred in any of the 31 patients during their follow-up planning CT scan and up to the commencement of their radiation. There were only slight increases in dysuria, urinary frequency, constipation, urinary retention and flatulence in 7 patients – none of which required intervention. One patient experienced dysuria, 3 patients experienced an increase in urinary frequency, 1 patient experienced mild constipation, 1 patient had a change in urinary retention and 2 patients experienced an increase in flatulence. In particular, no sepsis was recorded and no cases of rectal bleeding or gross haematuria requiring further intervention were reported. No other patients experienced adverse events in the week after the gold-seed insertion prior to radiotherapy treatment.

There was a weak relationship between pain score at deep anaesthetic infiltration and duration of procedure ($r2 = 0.01$, $p > 0.05$).

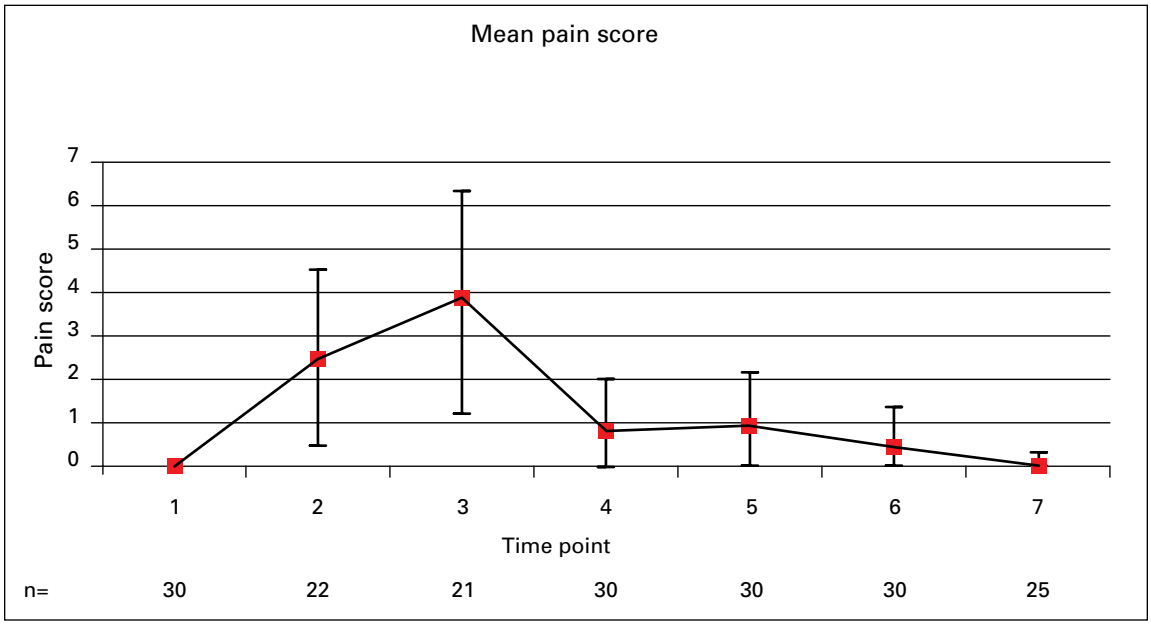

Fig 2. Mean visual analogue scale pain scores in patients at each time point during gold seed implantation (± standard error). The number of pain scores gathered at each time point are n=30, 22, 21, 30, 30, 30 and 25, respectively, at each consecutive time point. Time Point 1: Pre-procedure Pain; Time Point 2: Superficial Local Anesthesia; Time Point 3: Deep Local Anaesthesia; Time Point 4: Seed 1; Time Point 5: Seed 2; Time Point 6: Seed 3; Time Point 7: Post-procedure Pain.

Discussion

This study was a simple prospective study to determine patient pain tolerability with transperineal prostatic gold seed implantation in the absence of conscious sedation. As the study was exploratory in nature, no formal power calculations were performed a priori.

It was found that transperineal ultrasound-guided gold seed implantation without conscious sedation is well-tolerated. It is an outpatient procedure without the need for resource intensive postoperative monitoring.

The most significant increase in pain with the procedure is associated with the deep local anesthetic infiltration. This typically is felt as a sharp pain and settles within several seconds. One contributing factor may be inadequate time between superficial and deep infiltration, as diffusion of anesthetics from the superficial infiltration to the periapical prostatic neurovascular bundle requires time. This is evident from the negative association between duration of the procedure and increase in pain score noted at deep anesthetic infiltration.

Although some physicians adopted the other extreme of not using any anesthetics, local anesthesia is simple, can be done in the outpatient setting and has reduced risk compared with general anesthesia or conscious sedation. Irani and colleagues used a similar 10 point modified VAS to monitor pain for patients undergoing TRUS-guided prostate biopsy without local anesthesia. Although there may be some recall bias with under-reporting of the pain, 19% of patients in that study would not agree to undergo the procedure again without some form of anesthesia.[14] In a randomized double blind trial, Nash and colleagues showed local anesthestic infiltration around the vascular pedicle significantly reduces pain score.[15] Although Mutaguchi and colleagues asserted that intraprostatic infiltration was superior to periprostatic infiltration,[16] we routinely perform both periprostatic and intraprostatic infiltration as the latter is not associated with additional pain and adds little to the overall duration of the procedure. As long as one steers clear of the urethra, hematuria is uncommon.

A transperineal approach was also associated with minimal postoperative complications, although we recognize the small sample size. Interestingly, despite the risk of introducing pathogens, the transrectal approach in experienced hands was associated with good outcome and a low incidence of sepsis.[17] The OCC has explored the use of topical skin analgesic gel, but found it difficult to apply. Furthermore, intra-rectal analgesia is not associated with better tolerance.[18]

Conclusion

Transperineal ultrasound-guided gold seed implantation without conscious sedation is well-tolerated and associated with a low complication rate. It is a convenient outpatient procedure obviating the need for resource intensive post-operative monitoring.

Competing interests: None declared.

This paper has been peer-reviewed.

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