

## Prostatopubic fistula and osteomyelitis of the pubic bone as severe complication after salvage high intensity focused ultrasound for prostate cancer: report of two cases

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**High-intensity focused ultrasound has been used as an alternative treatment for prostate cancer, as both primary or salvage treatment. It is considered a minimally invasive treatment modality. We recently needed to care for two patients with severe osteomyelitis of the pubic bone as a result of a prostatopubic fistula, after they underwent salvage high-intensity focused ultrasound treatment post-radiotherapy.**

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### Introduction

High-intensity focused ultrasound (HIFU) is an ablative technique that, following the EAU guidelines, can be used in the primary treatment of prostate cancer (PCa) or as salvage therapy after failure of radiotherapy. It uses focused ultrasound waves to generate heat, leading to tissue destruction.<sup>1,2</sup>

Morbidity is considered low, with most frequent complications being erectile dysfunction, stress urinary incontinence, stricture, urinary tract infections (UTI) and urethrorectal fistula.<sup>3</sup>

Osteomyelitis of the pubic bone is a very rare complication after HIFU. In the literature, we only found two articles reporting this complication.<sup>4,5</sup> In this article, we present two more cases of pubic bone osteomyelitis following salvage HIFU after radiotherapy.

### Case report 1

In 2005, a 75-year old Caucasian male was diagnosed

with PCa, T1N0M0, Gleason score 6, iPSA 23 ng/ml for which he received EBRT in another hospital. Comorbidities included bilateral hip replacement.

In 2012, PSA rose to 3.8 ng/ml. 11C-Choline PET/CT showed a hypermetabolic focus in the prostate and in two lymph nodes. He underwent pelvic lymph node dissection and HIFU to the prostate in February 2013. In January 2014, he underwent transurethral bladder neck incision for stenosis, and in March, transurethral resection of necrotic debris in the prostatic urethra.

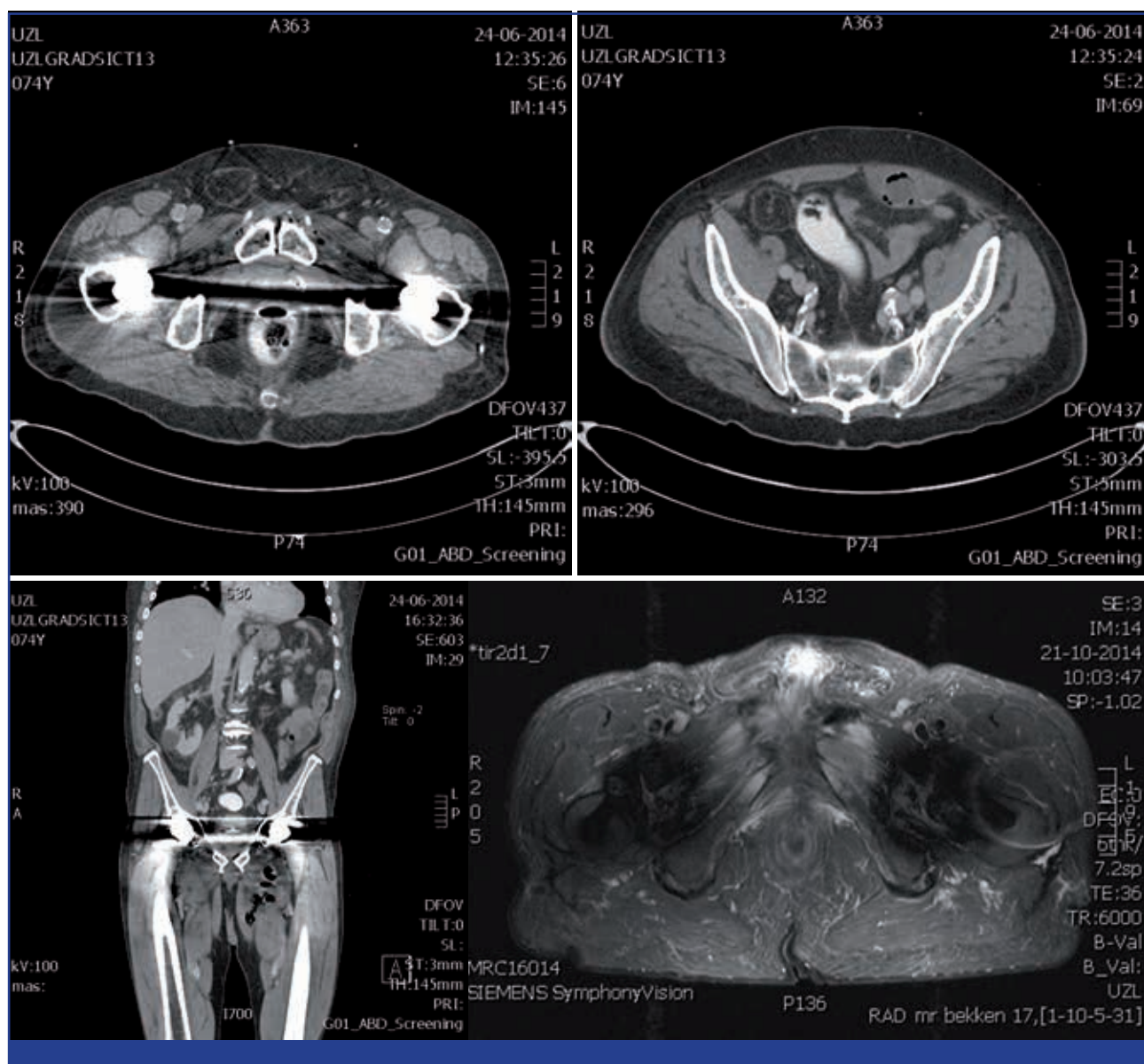
In June 2014, he was referred to our department because of persistent UTI and bilateral hip pain during gait. PSA was 1.2 ng/ml. Cystoscopy revealed necrotic tissue in the prostatic urethra. Afterwards the patient developed a severe urinary sepsis and was admitted to the ICU. A CT scan of the abdomen showed abscessation in the prostatic fossa, with air around the pubic symphysis and right pubic arch, and collections in the left adductor and m. rectus abdominis compartments.

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**Figure 1.** Patient 1: preoperative CT images of the pubic symphysis with free air (top left) collection in the m. rectus abdominis (top right), and adductor compartments (bottom left), MRI TIR image showing bone oedema of both pubic arches (bottom right).

Cystography confirmed urine leakage to the pubic bone. Hemocultures showed presence of *P. harei*. A suprapubic collection showed *Peptostreptococcus*, *P. harei*, *C. freundii* and *E. cloacae*.

The patient was put on temocillin, and later vancomycin and ornidazole. Because of limited clinical improvement, surgery was undertaken with resection of the right pubic bone and drainage of the suprapubic abscess, revealing extensive necrosis with connection between prostatic cavity and pubic bone. Two weeks later, a cystoprostatectomy with ileal conduit was performed. Pathology report showed extensive necrosis and viable PCa between prostate and bladder neck.

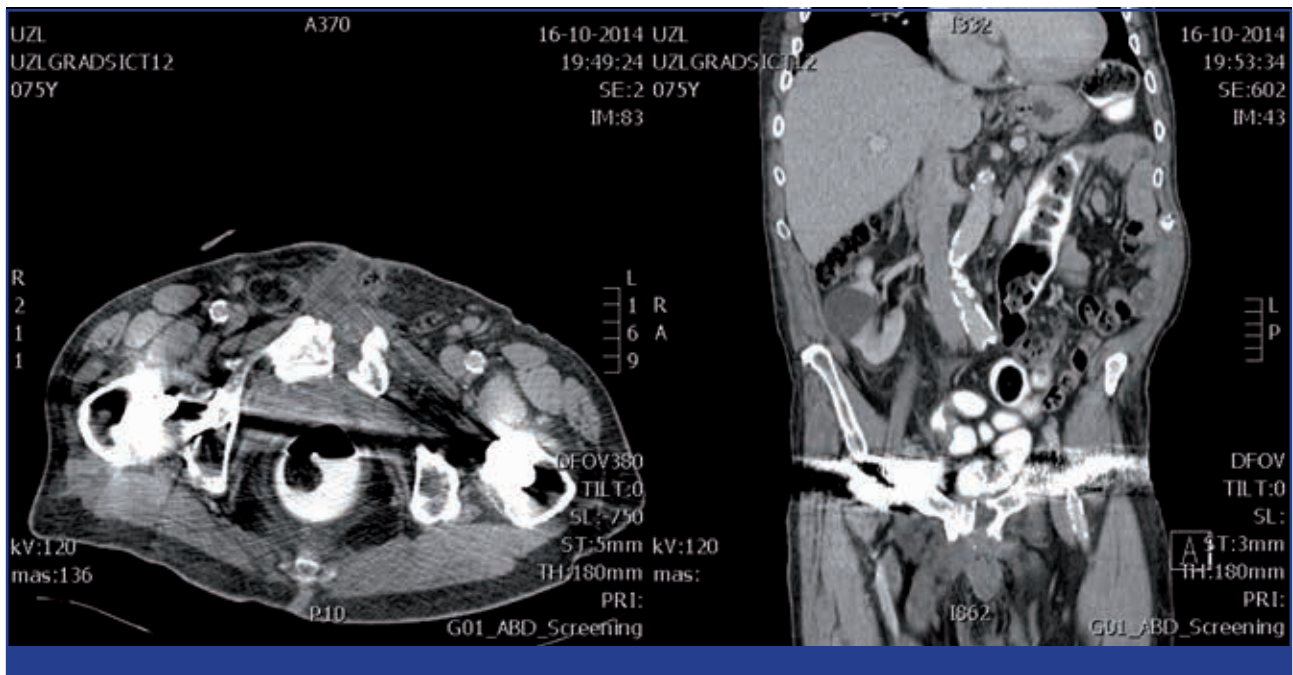
The patient was discharged from hospital seven weeks

after cystectomy with oral clindamycin for two months. His most recent PSA was 0.78 ng/ml, in December 2014.

## Case report 2

The second case is an 84-year old Caucasian male who was diagnosed with PCa in 2003, T3aN0M0, Gleason score 7, iPSA 15.54 ng/ml for which he received EBRT and androgen deprivation therapy for three years. Comorbidities included a spinal canal stenosis.

PSA became undetectable in 2004 and in 2009, it rose again to 2.80 ng/ml. 11C-Choline PET/CT confirmed local recurrence but no metastatic disease. New biopsies showed a Gleason score 4+5=9 PCa. In 2010,



**Figure 2.** Patient 1: CT imaging three months postoperatively, showing status post partial pubectomy.

salvage whole-gland HIFU was performed. Afterwards, PSA kept on rising and one year later, bicalutamide 150 mg was started because of a PSA of 10.47 ng/ml. PSA decreased to 1.09 ng/ml. Two and a half years after HIFU, a lithiasis in the prostatic urethra was removed and a balloon dilatation of the bladder neck was performed, with removal of multiple bladder stones. Meanwhile, PSA had risen up to 4.03 ng/ml, with multiple bone metastases on restaging. The patient was put on histrelin implant and denosumab. There were multiple admissions because of recurring urethral strictures and urinary retentions. In August 2014, clean intermittent self-catheterisation was initiated.

In August 2014, the patient presented in the emergency ward because of suprapubic pain and difficulties with self-catheterisation and pain during gait. Ultrasound showed a perivesical infiltration. Urine culture was negative and biochemically there was minor inflammation. He was initially treated with oral antibiotics and a temporary transurethral catheter, but because of recurrence, patient was admitted to the ward for IV antibiotics.

During hospitalisation, infection worsened, with evacuation of brown-coloured urine and an increase in inflammatory parameters. CT scan showed abscess formation and air bubbles in the suprapubic region, left m. rectus abdominis and bilateral adductor compartments, with suspicion of underlying prostatopubic fistula.

An urgent drainage of these abscesses was performed and the patient was admitted to the ICU. Three relook interventions were necessary. Wound cultures showed growth of *E. coli*, *A. urinae*, *P. disiens*, *A. turicensis*, *P. aeruginosa* and *S. aureus*. The patient was put on clindamycin, cefepime and ornidazole, later replaced by meropenem. A vacuum drainage system was applied to the wounds, however persisting urine leakage impeded adequate healing. The decision was made to perform a radical cystoprostatectomy with ileal conduit, and partial pubectomy with omental flap interposition on January 30<sup>th</sup>, 2015. Pathology report showed extensive necrosis and two foci of viable PCa.

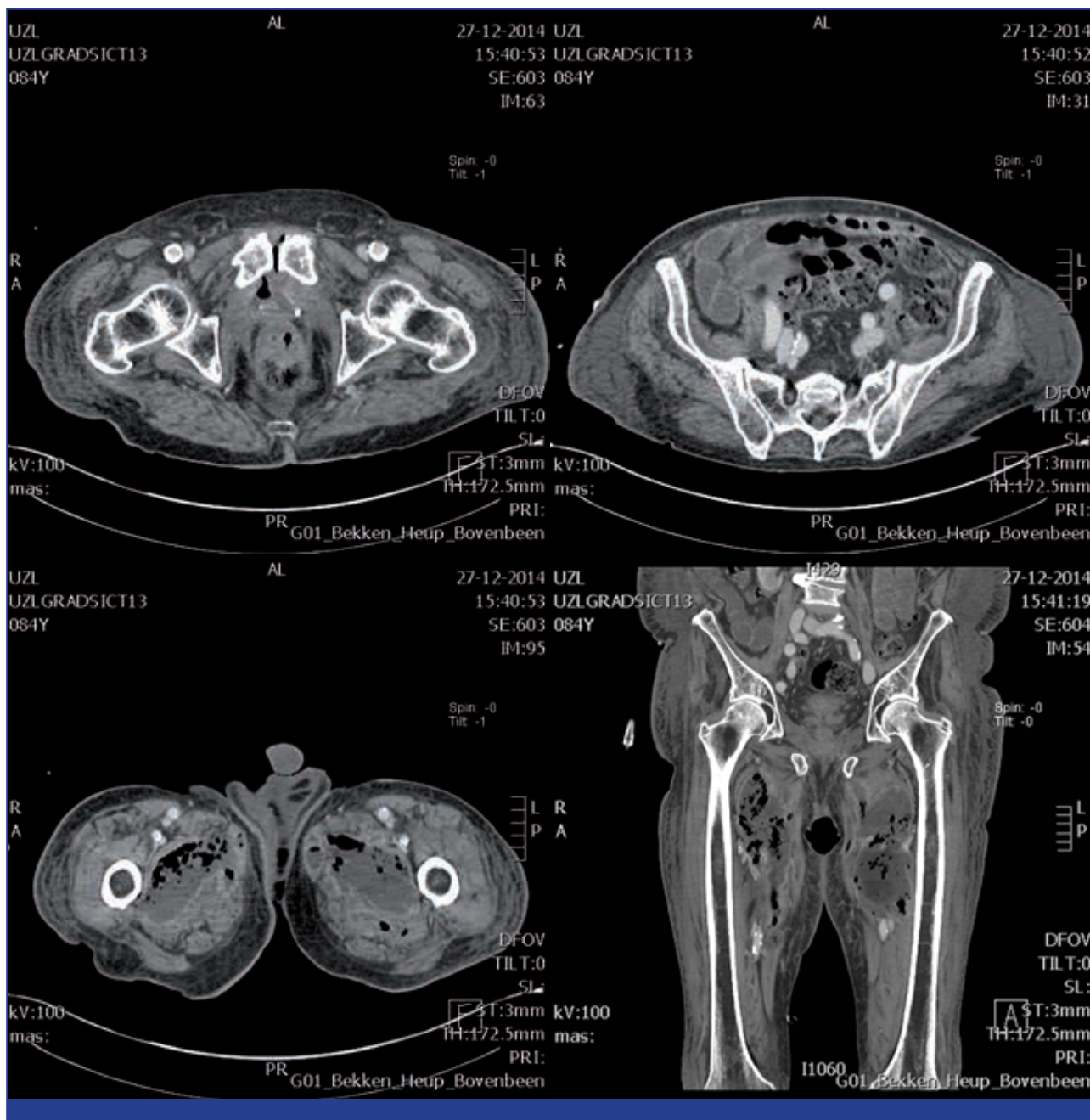
Four weeks after surgery, the patient went to a revalidation clinic with oral amoxicillin-clavulanate for six months and fluconazole for eight weeks. His most recent PSA was 1.93 ng/ml in March 2015.

## Discussion

HIFU is a treatment modality that uses focused high-energy ultrasound waves to ablate tissue. The procedure has been proposed as an alternative treatment for localised PCa when there are contraindications for radical prostatectomy or radiotherapy, or as salvage treatment after radiotherapy or radical prostatectomy.<sup>1,6-8</sup>

Literature shows 8-yr biochemical-free survival rates of 76%, 63%, and 57% for low-, intermediate-, and high-risk patients, respectively.<sup>6</sup> In salvage settings, rates range from 54% after one year to 17% after 5 years.<sup>3</sup>





**Figure 3.** Patient 2: preoperative CT images of the pubic symphysis with free air (top left), collection in the m. rectus abdominis (top right) and adductor compartments (bottom left and right).

Most common complications after HIFU are erectile dysfunction (55–70%), stress urinary incontinence (5–10%), stricture (9–12%), UTI (5–13%) and urethrorectal fistula (0–0.7%).<sup>3</sup> In salvage HIFU for radiorecurrent PCa, higher incontinence (28%), stricture (10%) and fistula rates (3%) have been reported.<sup>3</sup>

Currently, HIFU is not approved as a standard primary treatment in the EAU guidelines on PCa, as long-term follow-up is lacking, but it is accepted as an optional salvage treatment.<sup>2</sup> In the available literature, we only found two cases of prostatopubic fistula (PPF) resulting

in pubic bone osteomyelitis after salvage HIFU.<sup>4,5</sup> One was ultimately managed with bladder neck closure, the other patient underwent cystectomy with ileal conduit with partial symphysis excision. For diagnosis, MRI has been proposed as a gold standard, and for management, surgical debridement with or without diversion, complemented with antibiotics. These conditions should be managed in a multidisciplinary fashion.<sup>5</sup>

Similarly, Matsuhita et al. described twelve cases of pubovesical fistula, with ten out of twelve patients requiring cystectomy and urinary diversion.<sup>9</sup> However, these



**Figure 4.** Patient 2: clinical image after initial surgical drainage.

were patients treated with radical prostatectomy and/or radiotherapy, but not HIFU.

All reported cases of PPF after HIFU (our cases and the ones reported by Robison and Gupta) share some common characteristics; this combination probably contributed to prostatopubic fistulisation: all patients underwent radiotherapy, had bladder outlet problems and had one or multiple resections of residual tissue after HIFU. These factors can help create an environment with necrosis and delayed healing, and a propensity for extravasation of urine, contributing to fistulisation and pubic bone osteomyelitis.

Due to its low incidence, diagnosis of PPF is not readily made and can lead to a delay in treatment. Both our patients were diagnosed at a point where there was already an advanced disease with sepsis and abscess collections in the abdominal wall and adductor compartments. Both cases shared certain similarities in history and symptoms, most notably salvage HIFU after radiotherapy, recurring UTI and bilateral inguinal pain when walking. The first patient had had a bilateral hip replacement, possibly leading to ignoring the gait symptoms in making a final diagnosis. The second patient was known with a spinal canal stenosis. Also, there was only minor inflammation on initial presentation in this second patient, which initially responded well to oral antibiotics. As HIFU is often performed in elderly patients, the presence of gait problems is probably frequent, and their importance in making a diagnosis can be underestimated.

The diagnosis of both cases was made on a combination of clinical and biochemical data and ultimately, by CT scan. One patient also underwent cystography. We

agree that in isolated cases of pubic bone osteomyelitis, MRI is the preferred diagnostic tool. However, in these acute settings, CT scan is more readily available. Although in both cases, initial CT scans showed no active leakage of contrast from the bladder into the suprapubic area, diagnosis could be made indirectly based on patient history and the finding of gas bubbles in suprapubic, adductor and rectus muscle compartments.

In management, both patients only recovered after aggressive drainage of all collections. Partial pubectomy was performed at the time of drainage in the first patient and at the time of urinary diversion in the second patient. These interventions were performed in a multidisciplinary fashion, with experienced urologic, orthopaedic and reconstructive surgeons. Both patients were admitted to the ICU for several weeks and were put on broad-spectrum IV antibiotics. Both patients suffered from delayed wound healing and needed a cystoprostatectomy with urinary diversion to warrant a good recovery. Despite their age and the severity of the symptoms, both patients recovered well with resolution of inflammation, resolution of gait problems, good overall performance and a more or less stable oncological situation.

In both resection specimens, there was viable PCa tissue, illustrating the limitations of HIFU in oncological control. Moreover, in the first patient, PSA never decreased after HIFU, despite 11C-Choline PET/CT being negative for metastasis at that time.

## Conclusion

Although a rare complication, prostatopubic fistula and osteomyelitis of the pubic bone after salvage HIFU is a serious condition, requiring a multidisciplinary approach with aggressive surgical treatments and prolonged rehabilitation.

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## Key messages for clinical practice

1. Prostatopubic fistula after HIFU cases have a common history of radiorecurrent PCa and bladder outlet obstruction necessitating transurethral intervention.
2. Diagnosis should be suspected based on history, clinical and biochemical data. Pathognomonic sign is the finding of gas bubbles on CT scan, extending from the prostate to the pubic symphysis, suprapubic, and sometimes adductor and rectus muscle compartments.
3. Acute management requires surgical drainage, IV antibiotics and admission to an ICU. Final resolution is reached by cystoprostatectomy with urinary diversion and (partial) pubectomy.

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