INTRODUCTION
Locally confined tumours have the best prognosis after radical prostatectomy (RP), and MRI of the prostate may improve local staging; in at least one study it was better than a DRE in predicting treatment failure within 2 years [Urology 2000; 55: 572–7]. The objective of this study was to determine the accuracy of MRI in the local staging of prostate cancer in a series of RP.
PATIENTS AND METHODS

All patients (111) had an MRI before RP at a London teaching hospital between 1996 and 2002. In a retrospective analysis, the stage found on MRI and on histopathology was compared using sensitivity, specificity, positive and negative likelihood ratios.

RESULTS

The patients' characteristics were: (medians) PSA 9 ng/mL, biopsy and specimen Gleason score 6, and pathological stage pT2C (1992 TNM). The probability of extraprostatic extension was changed from 38% to 54% for a positive diagnosis, and reduced to 36% for a negative diagnosis on MRI. The diagnosis of either seminal vesicle invasion or lymph node involvement was unchanged. One of the two patients with lymph node involvement had tumour in the seminal vesicles, but the other did not. Both had perineural invasion in the RP specimen.

CONCLUSIONS

The diagnosis of extraprostatic extension on MRI increases the chance of extraprostatic extension pathologically, but is not useful in predicting either lymph node or seminal vesicle invasion. Other techniques are necessary to predict the latter conditions, which may include seminal vesicle biopsies before surgery.

INTRODUCTION

High-intensity focused ultrasound (HIFU) is a noninvasive therapeutic technique capable of thermally ablating precise volumes of tissue without damaging intervening biological structures. In urology, HIFU is currently being investigated for the treatment of localised prostate cancer (T1–2, Nx, M0). Clinical trials are in progress using transrectal devices that integrate HIFU transducers with separate diagnostic ultrasonography for image guidance. Whilst provisional results are challenging those obtained from radiation therapy, residual neoplastic foci are identified in some patients [Eur Urol 2001; 40: 124–9]. As TRUS imaging of prostate cancer is neither sensitive nor specific, some tumours may be undetected and therefore untreated. MRI, using an endorectal receiver coil, has been correlated with pathological findings and is considered to be the radiological 'gold standard'. We therefore incorporated this better imaging method with a HIFU transducer to create a transrectal device capable of mapping and ablating prostate cancer.

MATERIALS AND METHODS

A focused bowl transducer was designed for transrectal insertion, with characteristics selected to optimise tissue destruction. An MR endocoil was built around the constructed transducer and evaluated in a 0.5 T MR scanner. Subsequently, the conductive transducer surface was divided into four equal electrically isolated areas to reduce its effect on the MR image. The transducer was calibrated to obtain the acoustic field profile and the spatial peak intensity as a function of electrical power. The morphology and extent of HIFU-induced tissue necrosis was then studied in ex-vivo tissue.

RESULTS

Quartering the conductive transducer surface significantly increased the signal-to-noise ratio and homogeneity of the MR image. The three-dimensional acoustic (HIFU) field distribution had a quasi-ellipsoidal focal volume, of 10.2 × 3.1 × 1.5 mm (–6 dB). At 132 W electrical power the spatial peak intensity was 3080 W/cm². In ex-vivo tissue the lesions created at this power with 5-s exposures were clearly delineated, with dimensions of 8.1 × 1.7 × 1.3 mm (±6.5%).

CONCLUSION

A 'quartered' HIFU transducer capable of producing controlled and reproducible tissue necrosis was developed. Integration of an MR endocoil with this transducer created a single transrectal device capable of yielding high-quality MR images. In future clinical studies we aim to use this device to obtain better treatment results than those presently reported using TRUS-guided HIFU. This technique has the potential to be a viable alternative to the current first-line treatments for organ-confined prostate cancer.

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Early prostate cancer – which treatment do men prefer and why?

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INTRODUCTION
In 1997 we conducted a pilot randomized study comparing surgery and external beam radiotherapy (EBRT), which showed that men were unwilling to be randomized; we therefore continued as a patient preference study and report on men’s choice of treatment and their reasons in this ongoing study.

PATIENTS AND METHODS
Men with prostate cancer (T1/T2 N0 M0, PSA <20 ng/mL and Gleason <7) who were deemed suitable for prostatectomy were eligible for the study. Each man discussed the management options with a urologist, a clinical oncologist and a specialist nurse. Between 1997 and 2000 the choice was between prostatectomy and EBRT; after 2000 brachytherapy was included as a third option. Uniform written information was given to each man and the reason for their choice was recorded.

RESULTS
Since December 1997, 356 patients have been registered. Of these, 156 (43.8%) have chosen surgery, 130 (36.5%) EBRT and 61 (17.1%) brachytherapy. Nine patients (2.5%) opted for active surveillance; 327 patients (92%) could give a reason for their choice. For the ‘surgery’ patients, the most important deciding factor was ‘physical removal of cancer’, cited by 71% of men. For the brachytherapy patients, the important factor was ‘more convenient for lifestyle’ (51% of patients). For ‘radiotherapy’ patients, the reasons for choice were less clear, but the most common factors were ‘fear of other options’ (35%) and lifestyle considerations (23%).

CONCLUSION
Well-informed men prefer to make their own decision about treatment of their early prostate cancer and have clear reasons for doing so.

Quality of life (QoL) in men treated for early prostate cancer

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INTRODUCTION
The treatment of early prostate cancer carries a very good life expectancy and thus the QoL after treatment should be recorded accurately and considered fully when judging the success of treatment. We report on the impact of therapy on QoL in men offered either radical prostatectomy or external beam radiotherapy (EBRT) in our ongoing patient preference study.

PATIENTS AND METHODS
In all, 286 men were asked to complete a UCLA Prostate Cancer Index QoL Questionnaire (PCIQQ) before treatment, at 3 months afterwards, and annually thereafter. We compared the QoL at 3 months and 1 year for the entire group, with baseline values.

RESULTS
For the prostatectomy and EBRT groups respectively, the QoL score was completed at baseline, 3 months and 1 year by 125/156 (80%) and 101/130 (78%), 83/111 (75%) and 68/90 (76%), and 39/51 (76.5%) and 52/63 (82.5%). In the baseline measurements, two QoL variables were significantly poorer in the EBRT than in the surgical group. At 3 and 12 months mental health was better ($P=0.004$) than at baseline. Most variables of general wellbeing and prostate-specific symptoms were worse at 3 months but returned to baseline levels by 12 months in the vast majority of men. However, sexual function showed a persistent significant deterioration at 3 and 12 months.

CONCLUSION
There is a modest transient deterioration in QoL at 3 months after curative therapy of early prostate cancer. In most cases QoL returns to baseline levels by 12 months. There is a significant deterioration in sexual function which persists to 12 months.

Funding: Astra Zeneca provide financial support for Data Management
Radiotherapy in the treatment of prostate cancer: 5-year outcome analysis

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INTRODUCTION
In the absence of reliable data from a randomized controlled trial, the optimum treatment method for localised prostate cancer remains unproven. We review results from a large unselected cohort of men treated with radiotherapy alone.

PATIENTS AND METHODS
The outcome was analysed for 705 men with T1–T4N0M0 prostate cancer who received definitive conformal radiotherapy between 1995 and 1998. None of the patients received hormonal manipulation. The mean age (range) was 68 (49-84) years and the median pretreatment PSA 13 (0.6–270) ng/mL. The disease characteristics were: stage T1 in 125 (18%), T2 in 365 (52%), T3/4 in 215 (30%); Gleason 2–6 in 463 (66%) and Gleason 7–10 in 242 (34%); pretreatment PSA <10 ng/mL in 291 (41%), 10–20 in 228 (32%) and >20 in 186 (26%). The median (range) follow-up was 48 (1–82) months. Biochemical recurrence-free survival (bNED) was defined by the ASTRO consensus definition. Hypofractionated conformal radiotherapy using 50 Gy in 16 daily fractions over 22 days was delivered to the prostate plus base of the seminal vesicles.

RESULTS
The 5-year bNED survival was significantly associated (P<0.001) with pretreatment PSA level, stage and Gleason score. The 5-year bNED rates for the pretreatment characteristics were: 73% (PSA <10), 52% (>10–20), 35% (>20), 64% (stage T1/2), 38% (T3/4), 61% (Gleason score 2–6), 46% (>7). When patients were grouped into good (stage T1/2, PSA <10 ng/mL and Gleason score <7; 181 men), intermediate (one raised value; 247 men) or poor (two or more raised values; 277 men) prognostic groups, the bNED were respectively 82%, 56% and 39%. RTOG grade 3/4 late urinary or bowel toxicity was <1%.

CONCLUSION
These results indicate that for good prognosis patients, radical radiotherapy gives results similar to comparable surgical series with acceptable rates of toxicity. Patients in poorer prognostic groups, where there is increasing evidence of a radiotherapy dose effect, are now being treated in this centre to an escalated dose of 60 Gy in 20 fractions using intensity modulated radiotherapy.

A prospective study of PSA-free survival after 125I seed prostate brachytherapy: the first reported UK data

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INTRODUCTION
Since 1999 we have undertaken a prospective study of biochemical outcome for patients undergoing prostate brachytherapy (BXT) with >260 patients treated to date. We report early outcome data for patients with up to 46 months of follow-up.

PATIENTS AND METHODS
The biochemical outcome is reported for patients with >9 months of follow-up available (138, mean follow-up 25 months) or who died or had biochemical failure before this time. Patients received either BXT alone for low-risk disease (Gleason 7 or PSA 10–20 ng/mL or >T2b, group 2, 60 men, 44%) or a combination of 3 months of neoadjuvant androgen deprivation for intermediate risk disease (Gleason 7 or PSA 10–20 ng/mL or >T2b, group 2, 60 men, 44%) or a combination of 3 months of neoadjuvant androgen deprivation, 45 Gy EBRT and an 125I-BXT boost to the prostate for high-risk disease (Gleason ≥7, T3 or >one risk factor, group 3, 35 men, 25%).

RESULTS
No patients have died from prostate cancer to date and none have died with a rising PSA level. The mean PSA at 1, 2 and 3 years was 1.1, 0.46 and 0.38 ng/mL, respectively. Kaplan-Meier plots showed no significant difference in disease-free survival by treatment group and actuarial biochemical ‘no evidence of disease’ was 96% at 43 months.

CONCLUSION
Although it is clear that a longer follow-up will be needed before it can be confirmed that the results achieved in the USA have been duplicated, these early results are encouraging and suggest that BXT can be delivered safely in the UK.

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Cryoablation of the prostate – a prospective, consecutive series for recurrent adenocarcinoma

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INTRODUCTION
We report our experience of targeted cryoablation of the prostate as a salvage therapy in patients with recurrent adenocarcinoma after the failure of radical external beam radiotherapy.

PATIENTS AND METHODS
The study included 19 consecutive patients (mean age 66.7 years, SD 6.7) after failure of radical radiotherapy (18) or photodynamic therapy (one) for primary prostatic adenocarcinoma. Recurrence was detected by two consecutive rises in PSA and a prostatic biopsy in all cases. All were staged with a bone scan and MRI, and seven underwent lymph node sampling. A standard 4–8 cryoprobe approach was used under ultrasonographic control, with two or three freeze-thaw cycles, urethral warming and a periprostatic thermoprobe control in Denonvillier’s fascia, at the urethral sphincter and next to the neurovascular bundles bilaterally.

RESULTS
The mean (SD) time from primary treatment to cryoablation was 37.1 (20) months, the PSA level before treatment 9.4 (7.34) ng/mL, the Gleason score 6.53 (1.88), the mean inpatient stay 2 days, the mean PSA at 6 months 0.88 (1.5) ng/mL, and at 12 months 2.27 (2.34) ng/mL. The 1-year PSA-free survival was 12 of 19; in seven the treatment failed at 1 year, with two positive biopsies, four PSA rises, and one death (from other causes). Complications included early perineal discomfort and irritative LUTS, eight men with acute urinary retention, and five ‘mini’ TURPs. Seven men had stress incontinence, all had erectile dysfunction, one had deep vein thrombosis and two haematuria requiring readmission; none had a rectovesical fistula.

CONCLUSION
Targeted cryoablation of the prostate offers a 63% chance of a 1-year PSA-free survival as a salvage therapy, similar to published results from the USA. Improved technique minimises the severe side-effects, although LUTS and erectile dysfunction are common.

Cryoablation of the prostate: 10-year results of primary vs salvage therapy

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INTRODUCTION
The primary and secondary therapy for localized and locally advanced prostate cancer has caused considerable controversy in terms of efficacy and morbidity over the last decade. We report the 10-year follow-up in patients who underwent primary cryoablation for localized prostate cancer (66%) or secondary cryoablation for radiation failure (34%).

RESULTS
The clinical stages were T1 in 16 patients, T2 in 123 and T3 in 51. Risk factors were defined as stage ≤T2B, PSA >10 ng/mL and Gleason score ≤7. There were 96 high-risk patients (two or more risk factors), 76 at moderate (one risk factor) and 39 at low risk (no risk factor defined). The 10-year biochemical disease-free rates (PSA ≤0.2 ng/mL) were 67.5% for the low-risk, 51.7% for moderate risk and 28% for the high-risk groups. Complications in both the primary and radiation treatment failure group were obstructive uropathy (29.9% vs 33.8%) and urinary incontinence (11.8% vs 22.5%). Few patients were potent before therapy, but of those who were erectile dysfunction occurred in 11.8% vs 22.5%. The overall biopsy confirmed recurrence rate of 28.6% at 24 months was lower and did not correlate with the rate of detectable PSA at 10 years.

CONCLUSION
Targeted cryoablation of the prostate offers a 63% chance of a 1-year PSA-free survival as a salvage therapy, similar to published results from the USA. Improved technique minimises the severe side-effects, although LUTS and erectile dysfunction are common.
Salvage radiotherapy after radical prostatectomy

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INTRODUCTION
While the number of men referred for radiotherapy after radical prostatectomy (RP) is increasing, whether radiotherapy should be used in the adjuvant or salvage setting remains disputed. We reviewed the outcome of men receiving salvage radiotherapy for an increasing PSA level.

PATIENTS AND METHODS
Sixty-one men referred for salvage radiotherapy for biochemical relapse after RP were assessed retrospectively; 24 receiving hormonal therapy (HT) or with a follow-up of <12 months were excluded. Thus 37 men were identified (median age 64 years) with a median (range) preoperative PSA level of 11 (5.6–60) ng/mL, Gleason scores of <7 in 70%, 27 having positive surgical resection margins, eight seminal vesicle and one lymph node involvement. Radiotherapy was delivered conformally to the prostatic fossa, at 50–52.5 Gy in 20 fractions over 4 weeks. The date of failure after radiotherapy was defined by ASTRO consensus criteria or as the date of starting HT for a rising PSA level.

RESULTS
The median (range) time from surgery to radiotherapy was 31 (8–68) months; the median PSA level before radiotherapy was 2.9 (0.5–11.4) ng/mL. There was a PSA response after radiotherapy in 33 (89%) patients. At a median follow-up of 26 (13–68) months, 27 (80%) patients remained disease-free. The actuarial 3-year biochemical recurrence free rate was 64%. No patient developed metastases or died from prostate cancer. A PSA level of <2 ng/mL before radiotherapy predicted disease-free survival (P = 0.0083). There was no significant toxicity.

CONCLUSION
Salvage radiotherapy after RP achieved durable biochemical control in most patients. The outcome is better if radiotherapy is delivered when the PSA is <2 ng/mL. A policy of close monitoring after RP with early salvage radiotherapy is advocated.

89Strontium in early relapse of hormone-treated metastatic prostate cancer: efficacy, natural history and prognosis

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INTRODUCTION
89Strontium has been investigated in a randomized trial as a method of delaying the onset of pain in asymptomatic patients when PSA begins to increase after hormone treatment. The results also give an insight into the natural history of this phase of the disease.

PATIENTS AND METHODS
In all, 167 men with hormone-treated metastatic prostate cancer, in whom the PSA was rising from a nadir after treatment, were randomized to receive 89Sr (150 MBq) or a placebo injection.

RESULTS
In the placebo group the median time to development of pain was 168 days, with 18% free of pain at 1 year; in those receiving 89Sr it was 213 days, with 33% free of pain at 1 year (hazard ratio 0.606, 95% CI 0.414–0.889, P = 0.0103). The time to onset of pain was related to the metastatic load, as indicated by the Soloway score, (P < 0.001) and the nadir PSA (P = 0.030). The delay in onset of pain depended on the time from confirmation of the rise in PSA to injection (P < 0.001) and the time from diagnosis of bone metastases to injection (P = 0.0014).

CONCLUSIONS
The pain-free period after PSA relapse may last many months and this can be significantly increased by a single injection of 89Sr. The time to developing bone pain depends on disease load (Soloway score) and the nadir PSA. Delay in onset of pain relates to the rate of progression before treatment. Further experience may enable those patients most likely to benefit from 89Sr given on PSA relapse to be identified.

Funding: Amersham plc
Tamoxifen prophylaxis of bicalutamide-induced gynaecomastia and breast pain

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INTRODUCTION

Bicalutamide is increasingly used in prostate cancer as neo-adjuvant, adjuvant or monotherapy; gynaecomastia and breast pain are recognized complications of this treatment. Tamoxifen has been used successfully to treat established gynaecomastia; it has a half-life of 6 days. This study reports the prophylactic use of tamoxifen 20 mg once weekly.

PATIENTS AND METHODS

Sixty men commencing bicalutamide 150 mg once daily were randomized into treatment and control groups. The former started tamoxifen 20 mg once weekly simultaneously with the start of bicalutamide. Patients in both groups were monitored for side-effects at monthly intervals for 6 months. Baseline PSA and liver function tests (LFTs), and breast examination were recorded. PSA and LFTs were repeated monthly, together with physical measurement of breast disk size. All patients completed the study.

RESULTS

Six of 30 tamoxifen-treated patients developed mild gynaecomastia and breast tenderness, whereas 16 of 30 control patients developed moderate to severe gynaecomastia and tenderness. No adverse reactions to tamoxifen were noted. There was no difference in PSA response to bicalutamide in the two groups. No abnormality of liver function was observed in either group.

CONCLUSION

Once-weekly tamoxifen 20 mg significantly reduces the complications of gynaecomastia and breast tenderness associated with bicalutamide therapy, with no apparent adverse effects.