VOLUME 99 | SUPPLEMENT 4 | JUNE 2007

BJU INTERNATIONAL

BAUS Annual Meeting, 18–22 June 2007, SECC, Glasgow

Paper Sessions

Tuesday 19 June

2 Paper Session A
1330–1500 Hall 2
Governance and Management
Chairmen: Miss Janet Whiteway and Mr Oliver Wiseman
Papers 27 – 35

5 Paper Session B
1330–1430 Lomond Auditorium
Prostate Cancer – Treatment
Chairmen: Mr Declan Cahill and Professor Freddie Hamdy
Papers 36 – 40

6 Paper Session C
1430–1530 Lomond Auditorium
Basic Science – Oncology
Chairmen: Mr John Kelly and Professor James N'Dow
Papers 41–45

8 Paper Session D
1500–1630 Hall 2
Reconstruction
Chairmen: Professor Christopher Chapple and
Miss Tamsin Greenwell
Papers 46–52

Wednesday 20 June

10 Paper Session E
1330–1445 Hall 2
Renal Cancer
Chairmen: Mr Tim O'Brien and Mr David Shackley
Papers 80–85

11 Paper Session F
1500–1600 Lomond Auditorium
Basic Science – Physiology
Chairmen: Mr Marcus Drake and Professor Christopher Fry
Papers 86–90

13 Paper Session G
1445–1630 Lomond Auditorium
Bladder Cancer
Chairmen: Professor Dr Urs Studer and Mr Michael Wallace
Papers 91–98

Tuesday 19 June 1330–1500
Governance and Management
Chairmen: Janet Whiteway and Oliver Wiseman

27
Bankruptcy through biologicals in renal cancer
R. BAROD, N. COULL and T.S. O'BRIEN
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Introduction: Six thousand seven hundred people develop kidney cancer each year in the UK and 3600 will die of the disease. The prognosis for these patients may improve with the use of the new tyrosine kinase inhibitors (TKI), sorafenib and sunitinib. Trials of these drugs in a range of clinical settings are in progress. The drugs are very expensive (sorafenib £30,054; sunitinib £26,432 per annum) and this makes their affordability questionable, given that the total annual NHS budget for cancer drugs is around £600 million.
Methods: The costs of TKIs in RCC were estimated, both in patients with metastatic disease and in high risk adjuvant settings.
Results: The cost of TKIs for the treatment of metastatic disease is approximately £110 million in the first year. If patients with T2/T3 N0 disease were also treated, the additional cost would be £55 million.
Conclusions: The potential cost of TKIs in kidney cancer is astronomical and is likely to exceed 25% of the current total NHS budget for cancer drugs. Similar drugs are on the horizon for prostate and bladder cancer, so the affordability of biologicals could be the biggest issue in urological cancer in the next 20 years.

28
'Bottom-up' costing of minimally invasive treatments for prostate cancer in the NHS
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Introduction: Within the financially pressured NHS, surgical innovative technologies must consider their 'true' financial implications beyond pure clinical performance. Within Urology, example is made of the relatively recent implementation of minimally invasive treatments for organ-confined prostate cancer.
Methods: A 'bottom-up' costing was performed for both conventional and robot-assisted laparoscopic prostatectomy and high intensity focused ultrasound (HIFU). Comparison was made with 'bottom-up' costing of open prostatectomy and the agreed national tariff with and without adjustment for local market forces factor (MFF).
Results: See Table 1 below.
Conclusions: The current national tariff system does not distinguish between the three surgical approaches for radical prostatectomy and unadjusted reimbursement is made at £3701.00 irrespective of the higher 'true' costs of conventional laparoscopic and particularly robot-assisted approaches. This highlights an important health economical issue. Health care managers therefore have very difficult business decisions to make with regard to the implementation of innovative technology, such as minimally invasive treatments for prostate cancer when robust clinical outcome evidence is still awaited.

29
TRUS biopsy training – measuring competence?
R.A. HURLE, P. BOSE and N.J. FENN
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Introduction: The shortened Urology SpR training programme places an emphasis on diagnostic skills including Transrectal Ultrasound biopsies (TRUSB). Guidance on training and measuring competence is sparse. We assessed core length, cancer detection rates and complication rates within our mentored training programme as parameters suitable for measuring competence.
Patients and Methods: Three SpRs with no previous TRUSB experience were trained by two consultant urologists. PSA, prostate volume, number of cores taken and complications were recorded. Biopsy core lengths and histological findings were recorded independently by the pathologist. The first 25 biopsies performed by the SpRs were compared to 25 biopsies performed by the consultant urologists and a consultant radiologist. All 150 patients had a minimum of 8 cores taken using the same equipment.
Results: Patient demographics and results are shown overleaf. There were no unexpected complications.

TABLE 1: for 28

	Open prostatectomy	Laparoscopic prostatectomy	Robotic prostatectomy	HIFU
Total Cost per FCE('Bottom-up' costing)	£4024.01	£4916.80	£9390.74	£6667.49
National Tariff	£3701.00	£3701.00	£3701.00	£3701.00
National Tariff incl. MFF @ 1.446064	£5351.88	£5351.88	£5351.88	£5351.88
Increased Cost over National Tariff	£323.01	£1215.80	£5689.74	£2966.49
Increased Cost over MFF adjusted National Tariff	-£1327.87	-£435.08	£4038.86	£1315.61

TABLE 1: for 29

	Median	Age (years)	Median PSA (μg/l)	Median volume (cc)	Median core length (mm)	Cancer detection rate (%)
SpR	2	67	8.0	40.0	15.8	52
SpR	1	68	9.3	49.5	13.6	48
Consultant	3	71	11.0	55.0	15.9	40
Consultant	2	65	7.3	47.0	15.5	40
Consultant	1	66	7.4	67.0	14.5	40
SpR	3	68	10.0	55.0	14.1	40

Conclusions: SpRs can be trained to safely perform TRUSB to a similar standard (measured by the suggested parameters) as consultants within a structured training programme in as few as 25 patients.

30

The impact of 'Choose and Book' on urological outpatient attendance

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Introduction: It is generally assumed that by offering patients the choice of their appointment time and date, the electronic booking system (EBS) would improve the out-patients' attendance rate. The impact of this new system was determined by comparing the DNA rates for the different methods of referrals.
Methods: From April to November 2006, data on patient's age, sex, referral method and patient's attendance were collected and analysed for all new outpatient referrals.
Results: A total of 1952 referrals were made and the DNA rates for the different methods of referrals were as follows:

TABLE 1: for 30

Standard GP letter	15.3%	(n = 959)
Electronic booking system	18.9%	(n = 354)
Tertiary	24.3%	(n = 74)
Internal consultant	9.0%	(n = 256)
HSC205/Urgent	10.5%	(n = 124)
A&E	25.0%	(n = 119)
Other	13.6%	(n = 66)
Overall DNA rate (new)	15.7%	(n = 1952)
DNA for follow up patients (same period)	18.3%	(n = 4692)

Conclusion: The recent introduction of electronic bookings has not reduced the outpatient DNA rate. Paradoxically referrals made through the EBS had a higher DNA rate (18.9%) than those made through traditional means (15.3%). Although patients favour more choice in the NHS, their non-compliance with arrangements, made for their convenience, continues to be a dilemma which requires alternative management strategies.

31

An audit of the quality of urological intra-operative notes

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Introduction: Operation notes provide critical information directing post operative care for patients and planning appropriate future management.
Methods: Hundred randomly selected operation notes from our department were retrospectively reviewed from 2006. The contents of the notes were compared with Royal College of Surgeons (RCS) Guidelines for Good Surgical Practice relating to operation notes.
Results: Registrars wrote 79% of the operation notes. 25% of notes were missing the patient's name. 94% of entries were dated with none having start and end times of operations. All entries had names of the operating surgeon and assistant if present. 19% of case notes did not have a description of operative procedure and 88% did not have an indication for operation. Eight percent of operative notes had no post-operative instructions. 19% of notes were illegible. None were typed. 48% had a schematic diagram drawn by the writer.
Conclusion: The introduction of a typed operation note onto a central database as recommended by the RCS could improve post operative care for patients. This would also allow accurate coding of operations, providing improved information valuable to the planning of future service provision for urological units nationwide. Based on our findings, we are developing such a database.

32

NICE-improving outcome guidelines for urological cancers: are they achievable?

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Introduction: National Institute of Clinical Excellence (NICE) recommended improving outcome guidelines (IOG) in year 2002. We analysed the Hospital Episode Statistics data (HES) to evaluate the trends for pelvic radical urological surgery in England with context to these guidelines.
Materials and methods: HES database was extracted for pelvic urological cancer surgery [radical prostatectomy (RP) and radical cystectomy (RC)] for prostate and bladder cancer using ICD-10 and OPCS-4 codes (1998–2004). With reference to the NICE guidelines hospital and surgeons performing radical pelvic urological procedures (RP/RC/Both) were categorised into three groups.
Results: A total of 23,274 pelvic radical urological procedures (RP-14300, RC-8974) were performed over 7 year study period. Nearly 90% of hospitals and half of hospitals perform both RP and RC. Hospitals performing >50 procedures/year has increased from 14% (2002) to 19% (2004) and surgeons performing ≤5 procedures/year has decreased from 47% (2002) to 39% (2004). Though hospital and surgeon volume have increased over the study period, still 4/5th of hospitals are performing <50 procedures/year and 2/5th of surgeons performing ≤ five procedures/year.
Conclusions: NICE-IOG guidelines have shown marginal increase in the hospital and surgeon volume over the study period, but still 81% of hospitals are performing <50 radical pelvic urological procedures. Are these guidelines achievable?

33

The international lottery? A rationale for cost analysis in urological practice

N. COULL, A. SWEET and T. O.'BRIEN
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Introduction: Healthcare systems across Europe face one over-riding problem, i.e. how to afford the healthcare their citizens

TABLE 1: for 33

	UK	Germany	Spain	France	Italy	Sweden
Flexicystoscopy	626	35–57	47	782	57	185
TURBT	1057	2231	800–1500	3029	2061	1980
Cystectomy + reconstruction	10282	15419	9000–10000	9697	7222	15244

demand. In many countries, tariffs are one mechanism being used as an economic tool for cost containment. It is not known if procedure tariffs bear any relation to the true costs of performing the procedure. In many countries the method for determining tariffs is not transparent.

Methods: Tariffs for bladder cancer procedures in six European countries were compared. Information was retrieved from a combination of publicly available databases, and through direct questioning of local urological surgeons.

Results: Tariffs from various European countries are as shown. All tariffs are in Euro.

Conclusions: Variations in procedure tariffs across Europe for bladder cancer are breathtaking. There is an urgent need for high quality 'bottom-up' costing analyses both to determine the true cost of performing surgical procedures, and the overall costs of managing the disease.

34

Changes in department workload and registrar operating experience over a twelve year period

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Royal United Hospital, Bath, UK

Introduction: There have been considerable changes affecting higher surgical training in urology. The European Working Time Directive, centralisation of cancer services and Modernising Medical Careers have all had an impact on trainee experience. We examined the impact on operative experience by comparing logbooks of registrars working in one DGH over a 12-year period. We also looked at the change in overall workload over the same time.

Methods: Log books of four trainees working within the same department over a 12-year period were compared with respect to ten standard urological procedures. Two worked as single registrars whilst two worked together. Departmental records were used to compare operative workload over this period.

Results: See Table 1 (below).

Discussion: There has been the expected decrease in TURP but also a marked increase in stone work and the introduction of radical prostatectomy. Recent trainees gained increased exposure to day case and reasonable exposure to endoscopic procedures. This would appear to provide an excellent environment in which to train two consultant urologists.

TABLE 1: for 34

Registrar operations in 12 months:

	TURP	TURBT	Stent	Ureteroscopy	Orchidectomy	Exploration testis	circ	hydrocoele	open nephrectomy	RRP
93–94	213	80	22	5	5	7	16	7	8	0
02–03	77	25	30	19	9	7	22	11	17	20
04–05	50	42	15	38	2	8	45	45	10	4
04–05	26	41	17	15	4	4	26	26	9	11

Overall workload:

	TURP	TURBT	stent	Ureteroscopy	Orchidectomy	Exploration testis	circ	hydrocele	open nephrectomy	RRP
93–94	331	172	23	13	16	27	67	42	29	0
04–05	247	150	40	41	23	11	159	100	30	48
% change	-25	-13	+74	+215	+44	-59	+137	+138	+3	

35

A survey of urological experience amongst general surgery specialist registrars

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Introduction: A significant proportion of UK emergency surgical admissions are urological. General surgery SpRs are usually expected to competently initiate treatment for these patients. The aim of this study was to survey the urological experience of current general surgery SpRs and evaluate their perceived competency to manage acute urological emergencies.

Methods: General surgical SpRs registered with the Association of Surgeons in Training (ASiT) e-forum were invited to complete an online questionnaire. The questionnaire contained 14 questions and responses were collected online.

Results: Eighty-six general surgery SpRs completed the questionnaire, of which 61/86 (71%) were responsible for managing acute urological admissions. Of 51/86 (60%) respondents who had completed a formal postgraduate appointment in urology, 45% completed their post more than 5 years ago. 46/86 (53%) of general surgical registrars did not feel competent in managing acute urological emergencies. 63/86 (73%) of SpRs did not feel that it was appropriate for them to cover the urological take.

Discussion: Urological emergencies are commonly managed by General surgical SpRs, but the majority have had little recent urological training and do not feel competent to manage such patients. This study suggests that changes to surgical training are essential to ensure that surgeons are competent to manage urological patients and patient safety is protected.

Tuesday 19 June 1330–1430
Prostate Cancer – Treatment
Chairmen: Declan Cahill and Freddie Hamdy

36

What is the surgical outcome in men suitable for Active Surveillance?

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Introduction: Increasingly men with prostate cancer are assigned to active surveillance (AS). To reliably inform patients it is essential to know the outcome for all treatment options. We examined the surgical outcome in men who fulfil the Royal Marsden criteria for AS.
Patients: From our radical prostatectomy (RP) series, men aged 50–80 with PSA <15, biopsy Gleason score (GS) ≤7 and ≤50% positive cores were extracted with their pathological outcome. Men undergoing neo-adjuvant hormonal manipulation or salvage RP were excluded.
Results: Four hundred and twenty-five patients were included. 254 (60%) had organ-confined disease (*pT*2), 98 (23%) had extra-capsular extension (*pT*3a), nine (2%) had seminal vesicle involvement (*pT*3b), 18 (4%) had bladder neck invasion (*pT*4). Two (0.5%) had lymph node metastasis and 44 (10%) were unstageable. The RP GS was ≤6 in 221 (52%), seven in 190 (45%) and 8–10 in 14 (3%). 33% were upgraded at RP. Tumour volume was < 0.5 mls in 118 (28%), 0.5–1.5 mls in 208 (49%) and >1.5 mls in 99 (23%). 77 patients (18%) had insignificant cancers (GS ≤6, stage *pT*2 and volume <0.5 mls).
Conclusion: The vast majority considered for AS have significant prostate cancer and a substantial proportion have extra-prostatic disease.

37

10 years experience of radical perineal prostatectomy: a joint UK and South African series of 1100 patients

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Introduction: Only 5–10% of all RP are performed via the perineal approach. We present outcomes of a large series of RPP performed in the PSA era.
Methods: Between January 1996 and November 2006 we prospectively acquired data on 1100 consecutive RPP's performed by two surgeons. Peri-operative variables were recorded.
Results: A total of 929 patients with a minimum follow-up of 12 months were included. Mean follow-up 69 months (range 12–135). Mean age was 61 ± 16 years; median pre-operative PSA of 8 ± 6 ng/ml; mean operative time was 144 min (range 93–185); mean hospital stay of 3.2 ± 1.4 days; mean blood loss 334 ml; transfusion rate 3%; length of catheterization 14 days. Complications: wound infection/UTI 8%; anastomotic stricture 4%; rectal injury 0.006%; urine leak 0.01%; ureteric injury 0.001%. Staging: pT2 72%; T3 28%. Gleason grade: GG 2–4 7%; GG 5–7 84% and GG 8–10 9%. SV invasion in 9%. 27% of patients have suffered a PSA recurrence. Mean time to PSA failure was 20 months (median 12 months). Continence rate is 95% at 1 year. Potency rates for non, uni, and bilateral NS were 11%, 39% and 56% respectively.
Conclusion: RPP offers similar outcome to other surgical approaches with minimal morbidity and good cancer control rates.

38

Quality of life outcomes (QOL) post treatment for early localized prostate cancer: a comparison between radical prostatectomy (RRP) and high intensity focused ultrasound (HIFU)

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Introduction and objective: HIFU is rapidly emerging as a new treatment for early localized prostate cancer. It is described as a minimally invasive therapy with low morbidity, but how does it compare to the RRP.
Methods: We compared 30 patients who had received HIFU treatment for early localized prostate cancer with 30 patients having undergone a RRP at the same institution. We used the University of California Prostate Cancer Index (UCLA-PCI) to record patients QOL. Questionnaires were completed pre-operatively and at 3 months post-operatively and the difference in symptom score was evaluated.
Results: Patients electing to undergo HIFU were significantly older 68 versus 63 years (P = 0.009). There was no significant change in general health or health transition. There was a statistically significant deterioration in urine leakage, pad usage, urinary bother, erectile function and sexual bother in the RRP and HIFU groups pre and post operatively. However there was no significant difference between the two post-operative groups (Table 1).
Conclusion: This study shows that although HIFU is minimally invasive it still has considerable morbidity comparable to RRP. It may be that with further development of the technology and technique morbidity with this new technology may be further reduced. Table 1 Difference in the mean pre and post operative QOL scores and also the difference between the two treatment groups for five separate QOL indicators.

TABLE 1: for 38

	Difference in mean score between RRP and HIFU patient groups (*p*)		Difference in mean score pre and post treatment (*p*)	
	RRP	HIFU	Pre-op	Post-op
Urine leakage	53 (<0.001)	43 (<0.001)	2 (0.785)	-10 (0.276)
Pad usage	33 (<0.001)	25 (<0.001)	-3 (0.326)	-12 (0.09)
Urinary bother	22 (0.006)	25 (0.002)	-7 (0.34)	-4 (0.605)
Erectile dysfunction	53 (<0.001)	55 (<0.001)	-6 (0.54)	-3 (0.704)
Sexual bother	21 (0.018)	36 (<0.001)	-13 (0.239)	1 (0.94)

39

The use of trans-rectal high intensity focused ultrasound in salvage treatment for men who have failed primary radiation therapy of presumed organ confined prostate cancer

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Introduction: High intensity focused ultrasound (HIFU) has been proposed as a form of salvage treatment for men who have failed primary radiation therapy for prostate cancer.
Methods: Thirty-three men were treated over 15 months using the Sonablate®-500 device (Focus Surgery, IN, USA). All had biopsy confirmed prostate cancer recurrence following external beam radiotherapy and rising PSA. None were taking androgen deprivation therapy. Men received a single treatment session of HIFU only.
Results: The mean PSA before HIFU therapy was 7.73 ng/ml for the whole group (n = 33). In the men who have had at least 3 months follow up (n = 26) the mean PSA was 8.80 ng/ml. Three months after treatment seven men (n = 7) had unrecordable PSA levels, fourteen men (n = 14) had a PSA level less than 0.2 ng/ml, and twelve men (n = 12) had a PSA level of greater than 0.2 ng/ml.
Conclusions: Trans-rectal HIFU is able to significantly lower the PSA in a proportion of men who have previously undergone external beam radiation therapy for presumed organ confined prostate cancer. In this small cohort, 53.8% of men were able to achieve a PSA nadir of <0.2 ng/ml which has previously been shown to be associated with a good outcome.

40

3rd generation cryosurgery as salvage treatment for prostate cancer: single centre experience

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Objective: Third generation cryosurgery has established its role in treating localised prostate cancer and we are using cryosurgery as a salvage treatment for patients whose localised or locally advanced prostate cancer is relapsed following external beam radiotherapy or brachytherapy. The 44 patients who underwent this form of treatment were evaluated.
Materials and methods: Between October 2003 and October 2006 44 patients underwent treatment using an Argon-based 3rd generation cryotherapy system (ONCURA®). Prospective data were collected initially 3 monthly and subsequently 6 monthly followed for 30 months, median follow-up 12 months.
Results: A total of 60% of 10 patients maintained complete response (PSA ≤ 0.5 ng/ml) at 2 years and 80% of five patients at 30 months. From the patients with rising PSA five had re-biopsies, two of those were positive and three were negative for prostate cancer. 4 (9%) patients had TURP's for retention/LUTS, 3 (6.8%) developed fistula, 1 (2.2%) needed colostomy, 2 (4.5%) patients had persistent incontinence, two patients had cancer related deaths.
Conlcusion: Overall 59.5% of patients have maintained a complete response to the treatment. Although there are side effects of the treatment, these are comparable to the accepted published numbers. When radical treatment with radiotherapy fails, options for salvage treatment are very limited and in these situations cryosurgery is a valid acceptable option as a treatment for prostate cancer.

Tuesday 19 June 1430–1530
Basic Science – Oncology
Chairmen: John Kelly and James N'Dow

41

Do transcriptional repressors of E-cadherin have a role in bladder cancer?

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Introduction: Aberrant E-cadherin expression is an independent predictor of bladder cancer progression. E-cadherin function can be inhibited by gene mutation, promoter hypermethylation, or transcriptional repression. The latter has not been evaluated in bladder cancer.
Materials and methods: A panel of six bladder cancer cell lines was characterised for the expression of E-cadherin and its transcriptional repressors. Activity of E-cadherin repressors was determined using a luciferase transcriptional assay. Methylation of E-cadherin promoter in E-cadherin-negative cell lines was analysed by treatment with azadeoxycytidine, a demethylating agent. In bladder cancer specimens, E-cadherin and ZEB1 expression was assessed using standard immunohistochemistry.
Results: Bladder cancer cell lines belonged to two groups: epithelial, E-cadherin-positive and mesenchymal, E-cadherin-negative. Mesenchymal cell lines showed high levels of SIP1, Snail and ZEB1 transcription and mutating E2-boxes in these increased E-cadherin promoter activity. Azadeoxycytidine did not induce E-cadherin expression. In bladder tumours, an inverse correlation between E-cadherin and ZEB1 immunopositivity was shown.
Conclusions: We demonstrate for the first time that transcriptional repressors of E-cadherin play an active role in silencing E-cadherin in bladder cancer cell lines. In bladder tumours, E-cadherin and ZEB1 protein expression are inversely distributed.

42

The function of Fos-related antigen-1 (Fra-1) in transitional cell carcinoma (TCC) of the bladder

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Introduction: The 5 year survival rate of muscle-invasive bladder cancer is ~40%; accordingly, there is great interest in developing novel treatments. Fra-1, a member of the Fos family of proteins, has been implicated in several human cancers. Previously, we demonstrated that Fra-1 is present in the majority of muscle-invasive bladder cancers. Our objectives were to correlate Fra-1 levels with cell phenotype in bladder cancer cell lines and to determine the effect of modulating Fra-1 levels on phenotype and motility.

Methods: Expression of Fra-1, vimentin, and E-cadherin was assessed using Western Blot analysis. Cell motility was assessed using wound-healing assays. Fra-1 expression was modulated using transfection with a stabilised form of Fra-1 (HA-Fra-1Δ3) or with si-RNA to Fra-1.
Results: Cell lines positive for Fra-1 demonstrated a mesenchymal phenotype and increased cell motility. Knock-down of Fra-1 resulted in a change in phenotype and decreased cell motility, while enforced Fra-1 expression had opposing effects.
Conclusion: Fra-1 has a significant role in bladder cancer, acting as a regulator of phenotype and cell motility. As such, Fra-1 is a potential novel target in the treatment of bladder cancer patients. Si-RNA is an efficacious method of Fra-1 inhibition and may form the basis of future therapies.

43

Fos-related antigen-1 (Fra-1) – a putative target in muscle-invasive bladder cancer

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Introduction: Novel therapeutic targets are required in the treatment of muscle-invasive bladder cancer. One target, important in breast, colon and thyroid cancers, and which we have identified in muscle-invasive bladder cancer, is the Fos-related transcription factor Fra-1. C-Fos activity is modulated by phosphorylation of Ser374 by extracellular signal-related kinase 1/2 (ERK1/2) and Ser 362 by *p*90 ribosomal S6 kinase-1 (RSK1). If homologous sites in Fra-1 are similarly phosphorylated, targeting RSK1 and/or ERK1/2 are potential methods of modulating Fra-1. Here, we assess Fra-1 phosphorylation sites, and determine the effect of ERK1/2 inhibition on Fra-1 levels.
Methods: 32P-phosphomapping was performed in J82 cells transfected with wild-type and putative phosphosite mutant Fra-1 constructs; Western Blot analysis was performed on these mutants. J82 and RT112 cells transfected with wild-type Fra-1 were treated with the ERK1/2 inhibitor, U0126, and protein lysates subjected to Western Blot analysis.
Results: Fra-1 is phosphorylated at Ser 252 and Ser 265; substitution of either with alanine (mimicking non-phosphorylation) reduces Fra-1 levels, whereas substitution with aspartate (mimicking phosphorylation) increases Fra-1 levels. ERK1/2 inhibition decreases wild-type Fra-1 levels.
Conclusion: We suggest that it may be possible to target Fra-1, increasingly recognised as a key protein in a variety of cancers, using ERK1/2 and RSK1 inhibitors.

44

Down regulation of MT1-MMP leads to inhibition of invasion and increased expression of anti-migratory gene DKK3 in urothelial carcinoma cell line

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Introduction: Membrane-type I matrix metalloproteinase (MT1-MMP) a family member of zinc binding endopeptidases, plays a crucial role in tumour growth, invasion and metastasis. MT1-MMP has been shown to have a higher expression in the stromal compartment of the urothelial carcinoma (UC) cells. We aim to determine the role of MT1-MMP on invasion and its effect on gene expression in the invasive UC cell line (EJ28).
Materials and methods: Short interfering RNA technology was used to down regulate MT1-MMP in EJ28 cells. RNA was extracted and expression array profiling performed using a CRUK human cDNA platform. Candidate genes were validated both at RNA and protein levels. Invasion and wound healing assays were used to assess directional cell migration.
Results: Down regulation of MT1-MMP leads to decreased invasion ($P < 0.05$) as well as increased expression levels of the anti-migratory gene Dickkopf3 (DKK3). Furthermore, over-expression of DKK3 leads to a reduction in invasion and wound healing of wild type EJ28 cells.
Conclusion: MT1-MMP confers invasiveness in UC. Down regulation of MT1-MMP leads to loss of invasive phenotype and over-expression of DKK3 gene .We speculate that MT1-MMP, at least in part, exerts its pro-invasive effects by modulation of DKK3 gene.

45

Hoechst 33342 stem cell identification is a conserved and unified mechanism in urological cancers

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Introduction: Genetic mutations within adult human stem cells (SC) have been proposed to initiate and promote carcinogenesis. We have used the Hoechst 33342 dye efflux technique to isolate epithelial side-populations (SP) enriched for cells with SC characteristics and traits from urological tissues.
Materials and Methods: Hoechst 33342 profiles of CD45 -ve ($\pm$CD133 +ve) prostatic carcinoma (CaP), TCC bladder and RCC epithelial cells were generated by flow cytometry. Cell cycle status was established by Hoechst 33342 and Pyronin *Y* staining. Immunohistochemistry staining was performed for SC specific and lineage specific markers. Functionality was determined in colony-forming assays.
Results: A verapamil sensitive SP was isolated from all three urological malignancies, CaP (0.57 $\pm$ 0.11%), TCC (0.52 $\pm$ 0.49%) and RCC (5.9 $\pm$ 0.9%). Cell cycle analysis (TCC/RCC) showed that the SP had enhanced numbers of cells in G0 (TCC 11%, RCC 13.2 $\pm$ 3.6%). Cultures demonstrated enhanced colony-forming ability from the SP. Phenotypic analysis will be discussed.
Conclusion: An enriched SC population has now been isolated from the three commonest urological malignancies, providing strong evidence that the SP process is a unified mechanism. The multi-drug resistance pathways form the basis of the Hoechst 33342 dye efflux technique and potentially provide exciting therapeutic targets for the treatment of these important cancers.

Tuesday 19 June 1500–1630
Reconstruction
Chairmen: Christopher Chapple and Tamsin Greenwell

46

Hypospadias surgery in the developing world: 10 years, 600 cases

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Division of Paediatric Urology, Red Cross Children's Hospital, School of Child and Adolescent Health, University of Cape Town, South Africa

Aim: To review the experience with hypospadias surgery at Red Cross Children's Hospital, Cape Town.
Method: The operative database of the cases performed by one surgeon (LJ) was reviewed for demographic data, type of surgery and complications for the 10 year period 1994–2004.
Results: A total of 631 operations were performed. Complete data was available in 618 patients. The mean age was 43 months (4 years), with a median age of 34 months (2½ years) and a mode of 11 months. Operations used were MAGPI 12%, Matthieu 19%, Snodgrass 3%, Onlay island flap 18%, Duckett repair 26%, staged repair 6%, Megameatus intact prepuce 4%, Chordee only 13%. Surgery was complicated by urethrocutaneous fistula in 14%. 145 operations were done for fistula in 90 patients. Other revisions occurred in 37 patients (6%).
Conclusion: These data provide insight into the local experience with this complex surgery in South Africa.

47

Urethroplasty is a 23 hour stay procedure

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Institute of Urology, UCLH, London, UK

Introduction: Urethroplasty traditionally involved a hospital stay of about 1 week making it costly compared with endoscopic treatment.
Material and methods: Since October 2004 we have reduced our length of stay (LOS) in steps from 1 week to 23 h for all types of urethroplasty except abdomino-perineal urethroplasty.
Results: Re-admission rates and complication rates are not related to length of stay (LOS) and we have not had patient dissatisfaction as a result of a reduced hospital stay. The data presented in the table have been externally validated by Dr Foster.
Conclusions: Most urethroplasties can be performed as 23 hour procedures.

TABLE 1: for 47. All figures are number of patients/median length of stay (SD, 95% Confidence Interval).

Type of urethroplasty	April 03–Sept 04	Oct 04–Sept 05	Oct 05–Oct 06
Penile	91/6 (SD 2.98, CI 0.6)	47/4 (SD 2.94, CI 0.8)	74/1 (SD 1.36, CI 0.3)
Bulbar	48/6 (SD 0.78, CI 0.2)	44/3 (SD 1.83, CI 0.5)	59/1 (SD 0.8, CI 0.2)
Pelvic fracture	11/8 (SD 10.7, CI 6.4)	14/5 (SD 1.6, CI 1.8)	7/1 (SD 5.24, CI 3.8)

48

The outcome of single and two stage buccal graft reconstruction for glanular urethral strictures

M.F. LYNCH, Y. SMITH, P. HADWAY, C.M. CORBISHLEY, M.J.A. PERRY and N.A. WATKIN
Department of Urology, St George's Hospital, London, UK

Introduction: Recurrent meatal and glanular stricture disease can pose a difficult management problem. This may be complicated by BXO disease, co-existing hypospadias or previous hypospadias surgery. Two stage buccal mucosal graft reconstruction is generally advocated. We prospectively investigated the role of single stage buccal graft repairs in selected cases.
Patients and methods: Thirty six consecutive patients were treated over a 4 year period with either a single stage augmentation of the meatus/glanular urethra or a two stage substitution with buccal mucosal patch. The decision to perform single stage repairs was based on the following criteria: BXO disease not involving the glans spongiosus, stricture < 10 mm in length, absence of hypospadias. Failure was considered as recurrent symptoms or any flow curve abnormality on follow-up.
Results: Twelve patients had single stage repairs (five confirmed BXO, seven idiopathic). 24 had two stage repairs (16 confirmed BXO including three hypospadias failures, four hypospadias revisions, four idiopathic). Median follow up is 33 months. All single stage repairs and 23/24 two stage repairs are voiding normally.
Conclusion: Buccal mucosal grafting is a robust and reproducible surgical technique for the management of meatal and glanular urethral strictures. In selected cases a single stage repair can provide a satisfactory outcome.

49

Total phallic construction using the forearm free flap

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St. Peter Department of Andrology, Institute of Urology, UCLH, London, UK

Introduction: This is a series of 101 consecutive patients that had a total phallic reconstruction using the radial-artery-forearm-free-flap.
Patients and methods: The mean age was 35 years (22–54). The indications for surgery were micropenis (n = 7), female-to-male-transsexualism (n = 82) and following penile amputation (trauma = 5, cancer = 7). The procedure involves formation of the phallus from the non-dominant forearm with an incorporated urethra and microsurgical vascular and nerve anastamoses. The surgical outcome, complications and patients' satisfaction were recorded.
Results: After a mean follow up of 23 months (1–69), 95% of the patients were very satisfied with phallus size and cosmesis and 91% had phallus sensation. 66 of the 69 patients that have had the native and neourethra joined were able to void standing. Urethral fistulae and strictures requiring surgical correction occurred in 25% of cases. Other complications included arterial thrombosis requiring

re-explorated in two patients, venous thrombosis and phallus loss in two patients, contractures requiring split skin grafts in five patients. One patient developed a Volkman's contracture of the hand and persistent swelling and numbness were reported respectively by three and four patients.
Conclusion: Forearm-free-flap-phalloplasty yields excellent cosmetic and functional results for phallic construction. Despite multiple stages and revision surgery, the patient satisfaction is excellent.

50
Long-term bowel dysfunction after transposition of intestinal segments into the urinary tract
B.K. SOMANI, V. KUMAR, S. WONG, R. PICKARD and J. N'DOW
Aberdeen Royal Infirmary, Aberdeen, UK

Introduction: Bowel disturbance affects approximately 40% of patients following transposition of intestinal segments for bladder reconstruction. We have conducted a prospective longitudinal cohort study to determine whether such problems continue in the long-term.
Methods: We contacted 116 (76%) patients from an original group of 153 who had undergone bowel transposition surgery at least 10 years previously, and requested completion of symptom and quality of life (QoL) questionnaires.
Results: Questionnaires were received from 96 (63%) patients including 43 with ileal conduit; 17 with enterocystoplasty for idiopathic detrusor overactivity (DO); 18 with enterocystoplasty for neurogenic dysfunction and 18 with bladder replacement. Troublesome bowel symptoms were documented by up to 60% of patients with DO and half had impaired social functioning causing 24% to regret the original surgery. Although similar symptom prevalence was seen in the neurogenic group (50%), there was a lesser reduction in QoL. Symptoms were less common in patients with ileal conduit (19%) or bladder replacement (17%).
Conclusions: Bothersome bowel symptoms persist in a high proportion of patients 10 years following bladder augmentation and are associated with detrimental effects on QoL; particularly in those with DO many of whom regret the surgery. Alternative interventions for idiopathic DO are recommended.

51
Urolithiasis and enterocystoplasty – the role of biochemical and dietary factors
R. HAMID, W.G. ROBERTSON and C.R.J. WOODHOUSE
University College London Hospitals, London, UK

Introduction: The physical characteristics of intestinal reservoirs play an important part in stone formation. The dietary and biochemical factors have not been investigated. We investigated their role in urolithiasis in patients with enterocystoplasty.
Materials and methods: There were 15 stone formers and ten patients who have never formed stones. All were screened with a metabolic blood and urine screen and a 7 day diet. These data were compared and biochemical risk of stone formation calculated. An unpaired student *t* test was used with a *P* value of <0.05 taken as significant.
Results: The 24 h urine volume was 2.81 l/day in patients without and 1.99 l/day in those with stones (*P* 0.009), urinary pH was 6.46 versus 6.93 (*P* 0.005), urinary calcium was 2.8 versus 5.2 mmol/day (*P* 0.0008), citrate excretion was 2.13 versus 0.78 mmol/day (*P* 0.002). The biochemical risk for calcium oxalate and phosphate stone was lower in non-stone formers (*P* = 0.0002). The fluid intake was significantly higher (*P* = 0.04) in the non-stone forming group.
Conclusions: The use of bowel in urinary tract may not, on its own, increase the risk of stone formation. The stone formers are more prone due to the constituents of their urine and possibly the dietary habits.

52
Mechanism of lower urinary tract injury in pelvic fractures
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Institute of Urology, University College London Hospitals, London, UK

Introduction: The mechanisms of lower urinary tract injury (LUTI) in patients with pelvic ring fractures are poorly understood. We report further development of work presented 2 years ago.
Material and methods: We have reviewed the imaging studies of 168 patients with pelvic ring fractures. The pelvic fractures were classified according to the system described by Tile and correlated with observed types of LUTI.
Results: No patient with Tile Type-A(stable) pelvic-ring fracture sustained LUTI, neither did 75% of patients with Tile Type-B1(anterior-posterior compression), 67.5% of Tile Type-C(vertical shear) or 60% of Tile Type-B2(lateral compression) pelvic-ring fractures. When urethral injury does occur, there were distinct injury mechanisms observed: Lateral compression fractures cause either laceration injuries by a bone-spike of the bulbar urethra and/or bladder or crush injury of the bulbar urethra. Anterior posterior compression fractures cause avulsion or anterior tear of the membranous urethra. Vertical shear fractures cause disruption and distraction of the membranous urethra.
Conclusions: The type of pelvic fracture does not predict the presence of LUTI – most patients escape such injury probably because supporting ligaments rupture before the LUT is injured – but the mechanism of pelvic fracture can indicate the mechanism of urethral injury when it occurs.

Wednesday 20 June 1330–1445
Renal Cancer
Chairmen: Tim O'Brien and David Shackley

80

Open partial nephrectomy: a series of 141 patients

J.G. YOUNG, C.J. LUSCOMBE, C. LYNCH and D.M.A. WALLACE
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Introduction: Despite the advent of laparoscopic and other minimally invasive treatments for renal cancer, open partial nephrectomy (OPN) remains the gold standard for the treatment of appropriate patients: those who would be rendered anephric or likely to suffer renal insufficiency in the near future, and increasingly in the management of smaller unilateral tumours.
Patients and methods: We retrospectively reviewed the results of 141 open partial nephrectomies performed by one surgeon in a UK teaching hospital from 1992 to 2006. Partial nephrectomy was performed using renal ischaemia with cooling in 99%. Whenever possible the capsule was closed with a running suture after meticulous repair of vessels and collecting system.
Results: Data was available for 136 OPN. Indications for surgery were imperative in 73, elective in 59 and relative in four. Mean ischaemia time was 23 min. Mean length of stay was 10 days. Early post-operative complications occurred in 17 patients, including four cases of haemorrhage and four requiring temporary dialysis. Two procedures were converted to radical nephrectomy for hilar invasion. No urine fistulae occurred. Local recurrence occurred in five patients (in patients without VHL).
Conclusions: OPN with a standardised technique can provide excellent cancer control and preservation of renal function.

81

Open partial nephrectomy: the experience of one South London centre

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St. George's Hospital, London, UK

Introduction: We present a retrospective series of 80 patients who underwent an open partial nephrectomy at our institution between 1999 and 2006. 61% were incidental presentations. Of the 80 patients, 58 were elective and 22 were imperative cases.
Materials and methods: All cases were done by a single surgeon. Ice slush was used for cold ischaemia. Various haemostatic techniques were used. Perinephric drains were left for 1 week. Follow up was done according to local established protocol.
Results: All operations were completed successfully, with no intra-operative complications. The median warm and cold ischaemic times were 22.5 and 48 min respectively. Minimal change in pre and post op renal function occurred and no patient required permanent dialysis. Median tumour size was 34.2 mm. Malignant tumours comprised 80% (58% clear cell; 7.5% chromophobe; 15% papillary). There were 19 post-op complications, one requiring a total nephrectomy. Ten patients developed urine leaks, all closing with stenting. The number of complications in imperative cases was five (23%). There have been no tumour recurrences in any patients.
Conclusions: In the UK setting, the results indicate that our institution is a high volume centre with oncological outcomes, operative techniques and complications being comparable with other world renowned centres.

82

Laparoscopically assisted renal cryoablation for small renal tumours; results from a European multicentre study

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Introduction: Laparoscopic renal cryosurgery is a minimally invasive nephron sparing treatment option for small renal tumours. We present the clinical results from three European institutions.
Methods: Renal lesions <4 cm, suspicious for malignancy on CT or MRI, are suitable for cryosurgery. Under laparoscopic vision and with intracorporeal ultrasound guidance, the tumour is identified and a biopsy is taken before freezing (at least two freeze cycles). Persistent non-enhancement of the lesion (CT or MRI) is considered as successful ablation.
Results: Seventy suspicious renal masses in 66 patients, [mean age 67 (39–87), mean diameter 2.5 cm (1.3–4.1)] many of them with multiple co-morbidities (mean ASA 2.2) were treated. Six patients had solitary kidneys. Biopsy results included: 44 renal cell cancer, 11 oncocytomas, one angiomyolipoma, seven normal and two non-diagnostic (from five tumours no biopsy done). Mean hospital stay was 4.8 days (1–32). Two procedures were converted to open (hypercapnia, renal laceration). The majority had follow up CT or MRI available. One patient had nephrectomy at 6 months (residual tumour) and another, showing peripheral enhancement at 3 months, is being followed up.
Conclusion: Cryoablation is an attractive treatment option for small renal tumours, especially for patients with high co-morbidity, with encouraging initial results.

83

Comparison of laparoscopic versus open nephroureterectomy in the treatment of upper tract transitional cell cancer

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Aim: The outcome of patients undergoing ONU versus transperitoneal LNU for upper tract TCC between January 2002 and December 2005 was retrospectively evaluated.
Materials and methods: Operation records and patient records were reviewed. Seventy-one patients underwent ONU (data available on 60) while 55 had LNU (all data available). Patient follow up for a minimum of 1 year was available.
Results: The average patient age was seventy years and the male:female ratio 3:2. The conversion rate to ONU was 7.2%. The distal ureter was cored or resected in the majority of cases with an open bladder cuff excision in 11% (LNU) and 16% (ONU).

TABLE 1: for 83

	Open	Laparoscopic
Operating time (min)	182	198
Transfusion rate (%)	21	21.8
Complications (%)	21.6	18
Average/Range Hospital stay (days)	14 (4–70)	9 (3–50)
Stage T2 or less (%)	68	81
Complete excision (%)	86	96
Bladder recurrence (%)	11.6	4.5
Death from cancer (%)	16	4.5

Conclusion: LNU can be safely performed in patients with upper tract TCC with similar oncological outcomes to ONU. The clear benefit of LNU is a shorter hospital stay.

84

Avoiding major renal surgery for benign lesions – exploring the potential of immunohistochemistry

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Introduction: Distinguishing benign from malignant small renal lesions by imaging techniques is difficult. Consequently all published partial nephrectomy series include around 20–25% benign lesions. Confident pre-operative identification of benign lesions by examination of a needle biopsy could make surgery unnecessary or allow selection of a less invasive treatment modality e.g. radiofrequency ablation.

Materials and methods: Paraffin blocks from 40 renal tumours removed by surgery were examined by immunohistochemistry. Tumour type included ten each of oncocytoma, papillary renal cell carcinoma, clear cell carcinoma and chromophobe carcinoma. The panel of antibodies detected CK7, CK18, CD15, N-CAD, E-CAD and ESA.
Results: CK7, CD15 and ESA distinguished between oncocytoma and chromophobe carcinoma. No oncocytoma stained with either CK7 or ESA, however 8/10 (80%) stained positive for CD15. Conversely, 8/10 (80%) chromophobe carcinoma stained positive with CK7 and ESA but none stained for CD15. E-CAD and N-CAD were useful in distinguishing between oncocytoma and chromophobe carcinoma on the one hand and clear cell and papillary renal carcinoma on the other.
Conclusion: This immunohistochemical panel shows promise in differentiating benign and malignant renal lesions. The panel deserves evaluation prospectively on needle biopsy specimens.

85

Management of angiomyolipoma (AML) in a single centre

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Introduction: We aim to establish optimal management guidelines for patients with AML in our institute/region.

Materials and methods We did a retrospective study of 100 patients since 1998 with median follow-up 4 years. 69 patients had tuberous sclerosis complex (TSC) and were managed in our multidisciplinary genetic disorder team. Data was gathered from case notes, radiology and genetic databases.
Results: The majority were asymptomatic at presentation. Symptomatic presentations included pain, haematuria, visceral compression and spontaneous life threatening haemorrhage. Twenty patients received intervention. Main indications were spontaneous haemorrhage and size of AML. Sixteen patients underwent embolisation with the average tumour size 11 cm. Average reduction in tumour size was 28%; significant complications were seen in 30%. Two partial nephrectomies and four nephrectomies were carried out. Indications were failed embolisation, large tumour size and spontaneous haemorrhage. Two patients underwent radiofrequency ablation (RFA). Eighty patients with stable disease underwent surveillance scanning (ultrasound:method of choice). Median follow-up was 4 years.
Conclusions: Management of AML's in the TSC population is challenging. Our audit demonstrates that embolisation has limited efficacy in treating large tumours and has significant complications. Consequently RFA and systemic therapy are being trialed.

Wednesday 20 June 1500–1600
Basic Science – Physiology
Chairmen: Marcus Drake and Christopher Fry

86

Muscarinic acetylcholine receptor M1 (M1AChR) in the urothelium and suburothelium of normal and overactive human bladder: preliminary immunohistochemical data

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Institute of Neurology, University College London Hospitals; The National Hospital for Neurology and Neurosurgery, University College London Hospitals; Ealing Hospital NHS Trust, London, UK

Introduction: In animals M1AChR has been proposed as having a facilitatory role in the release of ACh and noradrenaline. Using immunohistochemistry we report for the first time the expression of M1AChR in human overactive bladders compared with controls.
Patients and methods: Flexible cystoscopic bladder biopsies obtained from 24 patients with neurogenic or idiopathic detrusor overactivity (NDO/IDO) before and after treatment with intradetrusor Botulinum toxin type A (BoNT/A) were immunostained with an antibody to M1AChR. Control biopsies were obtained from five patients investigated for asymptomatic microhaematuria.
Results: M1AChR immunoreactivity (IR) was identified in the urothelium and in suburothelial cells with long processes and fibre-like structures. Increased suburothelial nerve fibre IR was identified in controls compared to IDO ($P = 0.02$) and, to a lesser degree, NDO ($P = 0.06$) biopsies. Nerve fibre IR was unchanged after BoNT/A in the NDO subgroup, but was increased ($P = 0.026$) in the IDO group.

Conclusions: This is the first immunohistochemical evidence of the presence of M1AChR in the human overactive and normal bladder. Increased M1AChR IR in control bladders may promote the low facilitation of ACh release and reduced expression in DO bladders may balance the proposed increased expression of M2 and M3 receptors in the suburothelium.

87

The effect of β-adrenoceptor agonists and β3-adrenoceptor antagonist on detrusor contraction in the presence and absence of urothelium

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Introduction: We have recently shown that the urothelium appears to be involved in modulating the inhibitory effects of ß-adrenoceptor agonists on pig bladder. Pig bladder is known to be an excellent surrogate for human bladder, in terms of the similarity of pharmacological responses. The aim of the study was to determine which ß-adrenoceptor subtype mediates this effect.
Methods: Paired longitudinal strips of pig bladder dome were isolated, the urothelium was removed from one strip per pair and the strips were set up in organ baths. Relaxation experiments were performed by the cumulative addition of ß-adrenergic agonists (dobutamine, salbutamol, or BRL37344) to tissues pre-contracted with carbachol. The inhibitory effects (dobutamine, salbutamol, BRL37344, or isoprenaline with SRL59230A) were also studied by obtaining carbachol-response curves both in the absence and presence of urothelium.
Results: In relaxation experiments, the potency and maximal relaxation of the drugs were similar both in the absence and presence of the urothelium. In inhibition experiments, ß-adrenoceptor agonists caused rightward parallel shifts of the carbachol-response curves. In the presence of the urothelium there was a greater shift with BRL37344 only.
Conclusion: These data suggest that ß3-adrenoceptors are involved in mediating the inhibitory effects of ß-adrenoceptor agonists via the urothelium.

88

The effect of interferon-gamma on urothelial barrier function

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Jack Birch Unit of Molecular Carcinogenesis, Department of Biology, University of York; Pyrah Department of Urology, St James's University Hospital, Leeds, UK

Introduction: To investigate whether urothelial barrier function is susceptible to immune modulation, we used a differentiated normal human urothelial (NHU) culture model to study the effect of interferon-γ on barrier function and tight-junction composition.
Materials and methods: NHU cells were propagated as finite cell lines and induced to form a differentiated barrier epithelium by addition of serum and 2 mM calcium to the culture medium. Cultures were treated with interferon-γ for 72 h. Transepithelial electrical resistance (TER) and dextran permeability were measured as correlates of barrier function. Quantitative PCR was used to assess changes in claudins 2–5 and junctional adhesion molecule-1 (JAM-1) expression.
Results: TER increased in a dose-dependent manner following interferon-γ treatment in three independent cell lines. Mean TER increased by 34% (range 25–39%, $P < 0.0001$) and mean permeability to 4 kDa dextran reduced ($P < 0.01$) in response to 200 U/ml interferon-γ. Treatment with interferon-γ resulted in upregulation of claudins three and four and downregulation of JAM-1 transcripts.
Conclusion: This study suggests that urothelial barrier function is modulated by interferon-γ, indicating that the paracellular barrier may tighten in response to inflammation via modulation of the tight-junction. This *in vitro* model represents a novel platform for investigating the role of the urothelium in inflammatory bladder disorders.

89

Cholinergic control of prostate contractility mediated through smooth muscle M3 receptors

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Introduction: A cholinergic influence upon smooth muscle contractility may have implications for the management of BPH. This study investigated the effect of cholinergic agents on contractile activation, and their interaction with alpha-adrenoceptor agonists, using isolated human muscle strips. Muscarinic receptor subtypes within prostate tissue were localized by immunohistochemistry.
Methods: Tissue strips of human prostate were dissected, attached to an isometric force transducer and superfused with agonists and antagonists in a tissue bath preparation. Tissue for histology was snap-frozen and sectioned at 10 μm. Sections were labelled with specific antibodies to smooth muscle actin and M1, M2 and M3 receptors using the avidin-biotin peroxidase technique.
Results: Carbachol (3 μM) enhanced contractures to the alpha-agonist phenylephrine (PE, 3 μM) to 204 $\pm$ 91% of control and sensitised the response to PE. The use of selective muscarinic antagonists revealed greatest sensitivity to the M3-selective agent 4–DAMP. Immunohistochemistry revealed M3 receptors predominantly distributed in the stroma, coincident with SMA labelling.
Conclusions: Carbachol only generated a relatively small response alone, but could markedly augment the contractile response to phenylephrine. This synergistic mechanism appears to be predominantly mediated through the M3 receptor. M3 receptors were localised to the stromal compartment coincident with the smooth muscle distribution.

90

Dynamic changes in regional brain activity with sacral nerve stimulation in Fowler's syndrome

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National Hospital for Neurology and Neurosurgery and Institute of Neurology, London, UK

Introduction: Functional brain imaging using positron emission tomography suggests that sacral nerve stimulation (SNS) may restore voiding function and normalize desire-to-void by modulating brainstem and cortical activity. This is the first report on the feasibility and outcome of applying functional MRI to understand the mechanism of SNS in urinary retention.

Methods: Six females with retention were scanned in a 1.5 Tesla MRI scanner, following successful response to SNS test stimulation. Due to MRI safety concerns, the scans were performed following removal of the temporary electrodes, as a residual stimulation effect is known to exist. Block design of SNS on/off was applied, with full/empty bladder sessions. Subjects recorded changes in their desire-to-void. Analysis was performed using statistical parametric mapping software (significance at $P < 0.001$).
Results: Activity within midbrain and insula was positively correlated with a full bladder following SNS, whereas activity within anterior cingulate cortex and pons was negatively correlated.
Conclusions: The restoration of normal bladder filling sensations by SNS is reflected by increased activity in midbrain (primary relay center for bladder afferents) and insula (key centre for visceral sensation). Attenuation of activity in the pons may reflect a top-down inhibition of brainstem micturition reflexes for the maintenance of continence.

Wednesday 20 June 1445–1630
Bladder Cancer
Chairmen: Urs Studer and Michael Wallace

91
What is the contemporary standard for morbidity and outcome for radical pelvic surgery in the UK?
V.A.C. RAMANI and N.W. CLARKE
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Introduction: Morbidity and outcome for complex pelvic surgery has improved in recent years but there is still variation related to individual centre/unit and case volume. We have analysed a 35 year cohort of cases undergoing radical pelvic surgery to show the temporal changes in outcome and to determine a contemporary standard.
Methods: All cases undergoing radical pelvic surgery (radical cystectomies, total pelvic clearances) at a UK Cancer Centre from 1970 to 2005 were systematically analysed for post-operative complications and 30/60 day mortality. Audit was retrospective from 1970 to 1998 and prospective from 1999 to 2006. Cases were all treated at a centre by three urological oncologists with a high volume case load (>20 cystectomies each/year).
Results: A total of 769 cases were studied in cohorts 1970–79, 80–89, 90–99 and 2000–05. 30 and 60 day mortality for the cohorts were 13.1 and 15.5, 5.2 and 9.2, 4.6 and 5.6, and 1.8 and 3.6% respectively. Overall complication rate was 33% and this included infections (18%), prolonged Ileus (7.3%) and venous thrombosis (5.1%)
Conclusion: Morbidity from radical pelvic surgery has fallen considerably but remains significant. However the current 30 day mortality in a high volume centre has been systematically reduced to 1.8%.

92
Estimated GFR as a predictor of morbidity following radical cystectomy
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Introduction: To identify factors that predict morbidity following radical cystectomy and to determine whether intensive perioperative fluid management reduces duration of hospital stay.
Patients and methods: A single centre retrospective audit of 41 patients, mean age 67, who underwent radical cystectomy over 2 years. From June 2005, lithium dilution cardiac output (LiDCO) monitoring was introduced to optimize fluid balance. EGFR was calculated both pre and postoperatively.
Results: The overall complication rate was 37%. A pre-operative EGFR of <50 was associated with a 66% complication rate versus 33% if >50. The mean change between pre and day one postoperative EGFR was −10. When EGFR fell to <40 on day one ($n = 10$), patients were significantly more likely to have complications, 70% versus 28% ($P = 0.02$). EGFR better predicts potential complications than both ASA (44% ASA 3 versus 36% ASA 2) and P-POSSUM scores (mean score 9% versus 6%). In those without complications, the median duration of hospital stay was reduced from 19 to 14 days following introduction of LiDCO monitoring.
Conclusions: EGFR is a strong predictor of morbidity. Those with a drop in EGFR postoperatively may benefit from further high dependency care.

93
Rapid recovery surgery: the role of early enteral feeding to improve surgical outcome following radical cystectomy for invasive bladder cancer
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Introduction: Radical cystectomy has a high patient morbidity rate. Factors contributing to this include lengthy hospital stay, prolonged ileus and delayed feeding. We present the outcomes following early postoperative enteral feeding in patients undergoing radical cystectomy as part of a rapid recovery protocol.
Methods: Twenty-five patients were given protein rich supplements preoperatively and were recommenced on 30 mls/h supplements immediately postoperatively for the first day. By day three they were encouraged to drink freely and commence a light diet. A full diet commenced by day 5. Hospital stay and complications were compared to an age matched control group and data recorded prospectively.
Results: Mean hospital stay was 9 days (range 6–15) for the early feeding group compared to 18 days (range 9–43) for the controls. Complications in the early feeding group included wound infection ($n = 2$), prolonged lymph drainage ($n = 2$), pelvic collection ($n = 1$) and small bowel dehiscence ($n = 1$). In the control group complications included wound infection ($n = 2$), prolonged drainage ($n = 1$), ureteroileal leak ($n = 1$).
Conclusions: These results indicate that early feeding significantly reduces the length of hospital stay. Complication rates were similar in both groups. Early feeding is well tolerated following a radical cystectomy and a key factor in a rapid recovery protocol.

94

Troponin I elevation may predict silent myocardial ischaemia during radical cystectomy for muscle invasive bladder cancer

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Introduction and objectives: To reduce the substantial mortality and morbidity during radical cystectomy efforts may be made to minimise cardiac stress with beta-blockade or hypoxic preconditioning. We prospectively investigated troponin I as a marker of silent myocardial ischaemia.
Material and methods: Troponin I levels were measured at 12 h and 24 h post-operatively and compared with pre-operative levels in 30 patients undergoing cystectomy. Troponin I positive patients underwent serial 12-lead ECGs post-operatively.
Results: Troponin I elevations were found in 26% (8/30) of patients. Six of the troponin elevations (20%) were silent events. Of these, one patient developed a myocardial infarction. One patient had prolonged S-T depression indicating silent myocardial ischaemia and four patients had troponin I elevations without ECG changes or any other apparent causes.
Conclusions: Silent myocardial ischaemia or infarction appears to be a common occurrence after radical cystectomy and routine peri-operative troponin I monitoring may be indicated. Detection of silent myocardial ischemia predicts cardiac morbidity and mortality in postoperative patients and may contribute to the high 90-day mortality after radical cystectomy. Preventative measures following myocardial infarction are well established and very efficacious. Routine pre-operative stress testing, pre-operative beta-blockade or hypoxic preconditioning may be justified in all asymptomatic patients.

95

Lymphovascular invasion in bladder cancer: is it an important prognostic indicator?

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Aim: To determine the prognostic significance of lymphovascular invasion (LVI) in patients with transitional cell carcinoma (TCC) of the bladder who underwent radical cystectomy (RC).
Methods: Retrospective chart review showed 431 patients underwent RC between 1992 and 2006. Excluded were non-TCC, salvage procedures, unknown LVI-status and neoadjuvant treatment.
Results: Mean age of the cohort (n = 312) was 69 (±9) years. Mean follow-up was 34 (±34) months. LVI was reported in 115 (37.2%) patients. Prevalence of LVI increased with higher *T* stage (10%, 42%, 60% and 90% for *T*1, *T*2, *T*3 and *T*4 respectively, $P < 0.001$). 68% of node positive and 25% of node negative had LVI ($P < 0.001$). Overall 10 years recurrence free, overall, disease specific survival for LVI positive group was 56%, 31%, 38%, while LVI negative group had 74%, 54% and 78% respectively, with statistical significance (LogRank $P = 0.02$, $P = 0.0001$, $P = 0.001$). In node negative group LVI status significantly affected the overall and disease free survival ($P = 0.04$, $P = 0.001$). Multivariate analysis revealed *T*-stage ($P < 0.001$), lymphnode ($P = 0.002$) and LVI ($P = 0.04$) involvement were independent prognostic indicators for survival after RC.

TABLE 1: for 95

Factor	Category	LVI-Negative	LVI-Positive	*P*-value
Age	<70	95	62	
	>70	94	61	0.536
Gender	Male	160	97	
	Female	29	26	0.224
T stage	*T*1 or less	104	6	
	*T*2	44	32	
	*T*3	38	57	
	*T*4	3	28	0.000
N stage	Negative	179	71	
	Positive	10	52	0.000
Grade	*G*1	8	0	
	*G*2	8	2	
	*G*3	127	113	0.000
Concomitant CIS	No CIS	126	99	
	CIS	63	24	0.001

Conclusion: LVI is an important prognostic indicator of survival in bladder cancer patients undergoing radical cystectomy. These patients belong to a high risk group and may benefit from further therapy.

96

Abstract withdrawn

97

Intravesical gemcitabine in management of BCG refractory superficial transitional cell carcinoma (TCC) of urinary bladder

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Introduction: Incidence of bladder malignancy is increasing worldwide. The projected rise is 28% by 2010 for both sexes. Though intravesical adjuvant therapy with BCG is superior to any other immunotherapeutic/chemotherapeutic agents in reducing recurrences and disease progression, its real efficacy remains controversial as 1/3rd of these patients soon became BCG non-responders. Hence there is a need for an alternative intravesical agent for treatment of BCG non-responders. Our aim was to study the safety, efficacy, tolerability of intravesical Gemcitabine in managing BCG refractory patients.
Material and methods: Thirty five BCG refractory patients, 26 males and 9 females between 34 and 72 years of age were instilled 2000 mg of Gemcitabine in 50 ml of normal saline intravesically two weeks post tumor resection, for six consecutive weeks with mean follow up for 18 months with cystoscopies.
Result: Twenty-one patients (60%) showed no recurrences, 11 patients (31.4%) had superficial recurrences while three patients (8.6%) progressed to muscle invasiveness. Time to first recurrence was 11 months and to disease progression was 14 months with low and mild adverse event.
Conclusion: Gemcitabine fulfils all requirements as an alternative agent, in treating BCG refractory patients with tolerable adverse events, good patient compliance and highly effective in reducing tumor recurrences and disease progression.

98

Comparison of treatment outcome for radical surgery versus radical radiotherapy for invasive bladder cancer treated in a UK specialist treatment centre

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Purpose: Although there has been no direct randomised controlled comparison, surgery is often considered the gold standard despite its lack of bladder preservation and impact on patient quality of life. We conducted a retrospective analysis within a large university teaching hospital comparing outcomes between patients treated with either radical surgery or radiotherapy.
Patients and methods: Between March 1996 and December 2000, 189 patients were treated radically for muscle invasive bladder cancer. Data were collected from patient notes. Statistical analyses were performed using Kaplan–Meier methods and Cox proportional hazards regression analysis to compare radiotherapy and surgical outcome data.
Results: There was no difference in overall, cause-specific and distant recurrence-free survival at 7.5 years between the two groups despite the radiotherapy group being older (median age 75.1 years versus 68.2 years). There were 32 local recurrences in the radiotherapy group but no significant difference in distant recurrence-free survival between the two groups. In a more recent (2002–2006) cohort the median age of radiotherapy patients but not the cystectomy patients, was higher than in the 1996–2000 cohort (78.4 years versus 75.1 years for radiotherapy and 67.9 years versus 68.2 years for surgery).
Conclusion: Although patients undergoing radical cystectomy were significantly younger than radiotherapy patients, treatment modality did not influence survival. Bladder cancer patients are an increasingly elderly group. Radical radiotherapy is a viable treatment option for these patients with the advantage (over cystectomy) of organ preservation.