Programme Scientifique – Session I
Vendredi 7 novembre 2014

Validation of a microfluidic platform designed to test prostate cancer response to therapies

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Introduction et objectifs : The lethal and incurable form of prostate cancer (PC) is the castration resistant state that develops when patients progress while on hormone therapy. New strategies based on targeted drugs are increasingly gaining clinical acceptance, and may be appropriate throughout PC progression, including the later stages. However, an important consideration is matching the most appropriate drug to a patient's tumour characteristics. While response biomarkers (theranostics) are being developed to address this problem, a more direct solution would be to use a low-cost high throughput empirical testing platform. Recent developments in engineering have permitted the design and production of a new generation of microfluidic devices capable of trapping micrometer-size tumour samples and maintaining their viability over several days. We hypothesize that these devices are particularly well suited to meet the challenges of pre-clinical drug testing.

Matériels et méthodes : For the xenograft microbiopsy model, 22Rv1 or PC3 cells were mixed with matrigel, to allow the formation of denser tumours, prior to sub-cutaneous injection into the flank of male SCID mice. Mice were sacrificed before or when tumour size reached the limit point of 2500 mm3 and xenografts were immediately processed to produce numerous cylindrical microbiopsies (from 50 to 150 per tumour). Five xenograft microbiopsies were introduced into each microfluidic device and trapped in five independent wells. To follow the xenograft microbiopsy response to treatments, we applied 5 mM of CellTracker Green dye (live cell dye) for 40 minutes followed by 2 mM 7AAD (late apoptotic and dead cell dye) for an additional 20 minutes. Samples were observed directly in the microfluidic device by confocal microscopy. All xenograft microbiopsies were imaged in different z-sections (~ 10 mm step). For each z-section the mortality fraction (dead cells/total cells) was determined using an image-processing program (Matlab). Samples were then collected to quantify cell survival and apoptosis by fluorescence-activated cell sorting (FACS).

Résultats : Over the last year, we have developed a technique to precisely cut cylindrical tumour tissue samples (cylinders of 300 mm in diameter and 300 mm in length) by adapting traditional vibratome slicing techniques. We have also designed a microfluidic chip, with five independent microfluidic channels capable of holding up to 25 cylindrical PC samples in designated traps (five samples per channel). Samples can then be exposed to four specific chemotherapeutic agents or four different doses of the same agent plus a non-treated control. We demonstrated that xenograft microbiopsy sections obtained using our virbratome-based method can be loaded in the microsystems and maintained with high viability (75% to 95%) for up to seven days in such microsystems. We also demonstrated the feasibility of drug testing in our microsystems by the treatment of 22Rv1 and PC3 microbiopsies using different doses of docetaxel (from 1 nM to 100 nM).

Conclusions : With an increasing array of various therapeutics at hand, it is essential to classify or sort patients based on sound instruments and data when choosing a drug treatment. It is essential to maximize clinical response while minimizing treatment toxicities. Testing patient biopsy material should allow for direct empirical evaluation of therapeutic responses to a wide concentration and variety of agents. This rapid and directed approach would support clinical decision-making and allow the tailoring of therapeutic strategies for individual patients within an acceptable time frame. This would reduce not only the economic burden on the health care system but also the inconvenience and risk of exposing patients to drugs with little chance of success and the optimization of therapies in patients more likely to respond.

Reconstruction de tissu vaginal en utilisant la méthode d'auto-assemblage

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Introduction et objectifs : Les indications de chirurgies de reconstruction vulvovaginales varient grandement, de l'absence congénitale de vagin, aux malformations du sinus urogénital, d'extrophie cloacale voire d'exantérations oncologiques. Il n'existe pas de tissus parfais pour ces procédures, ainsi la disponibilité de tissu vaginal autologue serait souhaitable. Dans cette expérience, nous visions à définir les conditions de cultures idéales pour la confection d'un modèle de tissu vaginal en utilisant la méthode d'auto-assemblage. Ces tissus, produits seulement avec des cellules humaines et donc sans matériels exogènes, pourrait éventuellement être utilisé pour les procédures de reconstruction complètement autologues.

Matériels et méthodes : Des fibroblastes dermiques humains en cultures produisent des feuillets de matrice extracellulaire (stroma) en 4 semaines. Due à la non-disponibilité de cellules d'épithélmium vaginaux (CEV), des CEV immortalisées (VK2/E6E7 de ATCC) ont été utilises. Ces cellules ont été ensemencées sur le stroma puis cultivées pour une autre semaine dans le DH complet + facteur de croissance épithéliale (EGF), d'autres additifs et 10% de sérum de veau fétal (SVF). L'équivalent a ensuite été passé en interface air-liquide pendant 4 semaines pour favoriser la différentiation épithéliale. 36 équivalents ont été ainsi produits, utilisant 6 conditions de cultures différentes (n=6 par condition). Un équivalent par condition fut envoyé en histologie à 1 et 2 semaines, le reste allant en test de perméabilité et histologie à 4 semaines.

Résultats : L'histologie montre que, dans la majorité des conditions, le compartiment stromal est recouvert par un épithélium pluristratifié, confirmant l'habilité des CEV à adhérer et croître sur un stroma humain dans nos conditions de culture. Les additifs hormonaux, dont la progestérone et le B-oestradiol, ne modifient pas l'apparence histologique. L'épithélium croît également sans EGF. Des tests de perméabilité ont été effectués, démontrant un tissu comparable à un épithélium vaginal natif pour toutes les conditions, sauf lorsque cultivé sans SVF.

Conclusions : Nous présentons le premier modèle de tissus vaginaux reconstruits qui est 100% absent de matériels exogènes, dans ce domaine émergeant du génie tissulaire, ouvrant ainsi la voie à produire du tissu vaginal autologue humain. D'autres études sur le profil de différentiation de l'épithélium sont prévues dans un futur rapproché.

Prospective evaluation of pain during botulinum toxin A detrusor injection

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Introduction et objectifs : Botulinum toxin A (BTX-A) detrusor injection has been approved in 2011 by the FDA for the treatment of neurogenic detrusor overactivity. No publications have specifically addressed the pain related to this procedure. We aim to evaluate the level of pain during the different steps of BTX-A detrusor injections.

Matériels et méthodes : Between July and October 2013, we offered all our patients scheduled for BTX-A injections entry into our prospective study. During the standard procedure, the patients were asked to grade their level of pain according to a visual analogic scale 0–10 (VAS) at five different moments: arrival, urethral insertion, bladder filling, BTX-A injections and five minutes after removal of the instruments.

Résultats : Injections were performed in 36 patients (18 men, 18 women) with spinal cord injury (SCI) (69%), multiple sclerosis (MS) (22%), familial spastic paraparesis (FSPP) (6%), Huntington disease (HD) (3%), myelomeningocele (MMC) (3%).

In patients with complete SCI and MMC, injections were not adding more discomfort to the cystoscopy. For patients with MS and HD, cystoscopy had little impact on pain level compared to the injections (mean differential pain: 2 v/s 4,3). In patients with incomplete SCI, urethral manipulation seemed more painful with non-significant elevation of pain with BTX-A injections (mean differential pain: 3,8 v/s 1,4). The mean differential pain in patients with complete cervical (CCSCI) and dorsal SCI (CDSCI), incomplete dorsal SCI (IDSCI) and MCC were less than 1.

Conclusions : In patients with complete SCI and MMC, pain associated with the procedure was low. With incomplete SCI, pain can be better attributed to urethral manipulation than actual detrusor injections. For MS, FSPP and HD patients, detrusor injections explained their pain but their pain threshold seemed lower than the SCI population during urethral manipulation. Our goal now is to develop better strategies to minimize painful stimuli in this recurrent procedure.

Cost-effectiveness of MRI targeted biopsy of the prostate in a Canadian setting

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Introduction et objectifs : Systematic 12-core transrectal ultrasound-guided biopsy (TRUSGB) is the recommended approach to diagnose prostate cancer (PCa). Major limitations related to this "blind" approach include overdiagnosis and sampling errors leading to incorrect risk stratification and treatment allocation. Multiparametric MRI is able to accurately identify PCa lesions within the prostate. Compared to random TRUSGB, targeted biopsy using prebiopsy MRI to localize the tumour (MRITB) has been shown to detect significant PCa in an equivalent proportion of men, using 4 cores instead of 12, and avoiding the diagnosis of insignificant PCa and thus overtreatment in at least 10% of the cases. Costs and technical limitations still prevent this promising approach from becoming the new standard in PCa diagnosis. The goal of the present study was to assess whether the added initial costs related to MRI are balanced with the benefits of MRI targeted biopsy in a cost-effectiveness model using Canadian settings.

Matériels et méthodes : A conservative Markov model was developed to estimate the incremental cost-effectiveness ratio over 5- and 10-year periods. Standard TRUSGB and MRITB pathways were established. Study population consisted of men >50 years with a life expectancy >15 years and clinical suspicion of PCa. Based on previously published data, a decision analytic model taking into account the probability of men harboring PCa, the diagnostic accuracy of both procedures and the probability of being assigned to the various treatment options was developed. Medical (physician fees) and hospital costs (procedure fee, admission fee, tests and procedures) based on Canadian data were included. Possible MRITB advantages such as decreased number of biopsy, decreased infection rate and better risk stratification were not taken into account in order to avoid bias favoring this intervention.

Résultats : Following the standard systematic 12-core TRUSGB pathway, the calculated cumulative effects at 5 and 10 years were 4.92 and 9.51 years, respectively. When the MRITB pathway was considered, 5- and 10-years cumulative effects were 4.93 and 9.55 years, respectively. Costs related to the MRITB strategy were 14,590 and 31,638 CAD at 5 and 10 years, respectively, as compared to 13,686 and 32,552 CAD for the TRUSGB strategy. The 5-year incremental cost-effectiveness ratio (ICER) was 90'400 CAD/LYG. MRITB is the dominating strategy at 10 years with an ICER of -22'850 CAD/LYG.

Conclusions : Routine use of multiparametric MRI of the prostate in patients with elevated PSA is not associated with increased costs. While the benefits of MRITB are marginal at 5 years, the cost-effectiveness of this approach becomes significant at 10 years. Prospective trials assessing MRITB cost-effectiveness should confirm these results before it becomes the recommended approach.

Prevalence of microscopic hematuria and associated risk factors from the annual McGill Men's Health Day Study

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Introduction et objectifs : Microscopic hematuria is a common incidental finding in routine urinalysis. Up to 5% of these patients will present a urinary tract malignancy. There are currently no clear recommendations concerning the use of urinalysis as a screening tool in the general population. The aim of this study was to identify the prevalence of microscopic hematuria in the general population presenting to an annual Men's Health Day Clinic and identify the risk factors associated with microscopic hematuria.

Matériels et méthodes : This retrospective study was completed using data collected at McGill's annual Men's Health Day clinic from 2008 to 2012. Patient reported questionnaire, basic physical exam including digital rectal exam, basic blood tests and urine dip stick data was examined. Data was analyzed using SPSS using chi-square, fisher exact test, regression analysis and student t-test as appropriate. 95% confidence intervals were used.

Résultats : 789 patients were included. 691 had urine dipstick done. 69 (10%) had hematuria on urine dipstick. Among these, previous history of hematuria was positively correlated to current hematuria (OR 6, CI 2.5–14.5). Average age in both groups was 56 years. Diabetes was positively associated with hematuria (OR 3.7, CI 1.7–8). There was no correlation identified with smoking, age, hypertension, previous malignancy, maximum exercise tolerance, body mass index (BMI), prostate specific antigen (PSA), International Prostate Symptom Score (IPSS) or Overactive Bladder-8 (OAB8) questionnaire score.

Conclusions : Microscopic hematuria on urine dipstick is a prevalent condition among the general population. Microscopic hematuria showed positive correlation with a previous history of hematuria and with diabetes. However, there were no associations to other proven risk factors of hematuria and urothelial malignancy such as smoking and age. It also showed no association to lower urinary tract symptoms assessed with OAB and IPSS scores. Based on the presented data, urine dipstick cannot be recommended as a screening test for the general population.

Nephrectomie partielle assistée par robot : quels sont les bénéfices suivant l'experience initiale?

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Introduction et objectifs : La néphrectomie partielle (NP) représente le traitement de choix pour les tumeurs de moins de 7cm localisées au rein. Comparé à la NP à ciel ouvert, l'approche coelioscopique à permis de réduire les pertes sanguines, la morbidité ainsi que la durée du séjour hospitalier en maintenant des résultats oncologiques équivalents à moyen terme. Toutefois, des temps d'ischémie chaude (TIC) prolongés ont été rapportés. Grâce aux 7 degrés de liberté, à la vision tridimentionnelle ainsi qu'à la filtration des tremblements, la NP assistée par robot

(NPR) à permis de surmonter cette limitation. Des résultats oncologiques et fonctionnels prometteurs ont été rapportés par des centres d'expertise à casuistique élevée, le plus souvent sans prendre en considération la courbe d'apprentissage. L'objectif de cette étude est de rapporter notre expérience préliminaire avec la NPR en comparant les 55 premiers cas aux 50 suivants dans un centre de casuistique moyenne.
Matériels et méthodes : De janvier 2011 à avril 2014, les patients bénéficiant d'une NPR sont inclus dans cette étude à laquelle 3 chirurgiens aux expériences laparoscopique et robotique diverses participent. Il est décidé a priori de comparer la première moitié de la cohorte (groupe 1, expérience initiale) à la deuxième (groupe 2, expérience tardive). Pour chaque patient, ses caractéristiques préopératoires, le score de nephrométrie RENAL, les paramètres intraopératoires ainsi que les données anatomopathologiques et les complications sont relevés dans une base de données. La NPR est réalisée de manière standard comme décrit précédemment. La fonction rénale est calculée selon la formule Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) en préopératoire, à J2 postopératoire et durant le suivi clinique (1–3 mois).
Résultats : Cent-cinq patients sont inclus dans la présente analyse. Le ratio homme: femme est de 63:42. L'âge moyen(écart-type) est de 60(13) ans tandis que le BMI est de 28(7) kg/m2. Il n'y a pas de différence significative d'âge, de sexe, de BMI, de score ASA ou de fonction rénale préopératoire entre le groupe 1 (n=55) et 2 (n=50). Le temps opératoire (203(62) et 188(48) minutes, respectivement; p=0.37) ainsi que les pertes sanguines (243(225) et 259(241)ml, respectivement; p=0.79) sont similaires entre le groupe 1 et 2. Le TIC passe de 25(10) minutes dans le groupe initial à 20(8) minutes dans le second (p=0.02). La taille tumourale et le score de néphrometrie sont similaires entre les deux groupes (40(22) versus (36(19) mm ; p=0.41 et 7.5(2.0) versus 7.3(1.9); p=0.48). Dans 82% des cas la lésion est maligne. La distribution des sous-groupes histologiques est semblable. Nous observons une tendance vers une diminution des marges positives dans le groupe 2 (1 versus 5, p=0.1). La diminution de la fonction rénale est comparable dans les deux groupes. Le taux de complications initial est de 21% (22/105) est diminué de manière significative dans les derniers 50 cas (12%; p=0.03), permettant une diminution de la durée du séjour de 3.1(1.8) à 2.3(0.9) (p=0.01).
Conclusions : Après une expérience initiale de 55 NPR, nous constatons une diminution significative du TIC, des complications et de la durée du séjour, ainsi qu'une tendance vers un taux de marge positives réduit. Les résultats obtenus après l'expérience initiale sont comparables à ceux rapport par les centres de casuistique élevée.

The role of HMGB1 in the combination therapy of gemcitabine and radiation in bladder cancer

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Introduction et objectifs : Radical cystectomy is the gold standard treatment for Muscle Invasive Bladder Cancer. However, it causes a serious impact in the quality of life of the patients. Radiation Therapy when combined with radio-sensitizing chemotherapy is an attractive alternative as it offers bladder preservation allowing for normal urinary and sexual functions. However, lack of local control and dose dependent toxicity are the main drawbacks of the combination therapy. As such, there is an imperative need to improve radio-sensitization of bladder cancer to the combined treatment. As HMGB1 has been found to be associated with DNA damage response and chronic inflammation pathways of radiation resistance, it is a strong candidate for this study. Currently, as Gemcitabine is utilized as an adjuvant in bladder cancer radiation therapy, we want to investigate the role of HMGB1 in the response to this combination.
Matériels et méthodes : The expression of HMGB1 among different bladder cancer cell lines was analyzed by mRNA quantification and Protein quantification. The mean growth inhibition to Gemcitabine was assessed by colorimetric assays of cellular viability by exposing the cells to varying doses of Gemcitabine (5 nMol-5000 nMol) for 48 hours. To assess the effect of the combination therapy, Clonogenic assay was done. Cells were exposed to the mean growth inhibition dose of Gemcitabine for 6 hours followed by varying doses of Radiation (2–8 Gy).
Résultats : HMGB1 expression was analyzed in eight urothelial carcinoma cell lines. Amongst all, UM-UC3 and UM-UC5 had the highest expression while 253J-BV had the lowest expression of HMGB1. Using cell viability assay, the mean growth inhibition to Gemcitabine was determined and it showed that UM-UC3 and UM-UC5 were fairly resistant to Gemcitabine (≃ 100 nMol) while 253J-BV was quite sensitive (≃ 5 nMol). Furthermore, to evaluate the ability of HMGB1 to predict the response of the combination therapy (Gemcitabine and Radiation), knockdown of HMGB1 in UM-UC3 was done using lentiviral shRNA system. Our preliminary results from Clonogenic assay show that knockdown of shHMGB1 resulted in a dose modifying factor (DMF) of 1.37 for a survival fraction of 0.5. These findings strongly suggest that knockdown of HMGB1 leads to increased sensitivity of bladder cancer cells to the combination therapy.
Conclusions : We are currently evaluating the role of HMGB1 in pathways that lead to bladder cancer cells becoming resistant to combination therapy. Also, to validate these results we are conducting an in vivo xenograft study in which we would be evaluating the effect of HMGB1 knockdown and its response to the combination therapy. Finally, our in vitro results strongly suggest that HMGB1 can be a good marker for predicting bladder cancer response to the combination therapy of Gemcitabine and Radiation.

Fabrication d'un substitut urétral en genie tissulaire : un grand pas vers les tests pré-cliniques chez le lapin

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Introduction et objectifs : Pour la plupart des pathologies urologiques nécessitant une reconstruction tissulaire, les nombreuses complications reliées aux procédures chirurgicales et la faible quantité de tissu disponible, soulèvent notre intérêt pour le développement d'un substitut urétral. Nous proposons un substitut humain, produit par la méthode d'auto-assemblage, lequel est totalement autologue et exempt de biomatériaux. Cette technique permet la production d'un matériel biocompatible, au potentiel non-immunogénique pour les chirurgies de reconstruction. Notre modèle est en mesure d'atteindre jusqu'à maintenant de hauts standards de qualité. Cependant, avant le passage vers les tests cliniques, des implantations animales devront être complétées. Le but de cette étude est donc de créer un modèle lagomorphe de substitut urétral autologue à partir de cellules jamais cultivées auparavant, pour l'implantation lors d'études précliniques.
Matériels et méthodes : Les extractions cellulaires sont exécutées à partir de biopsies de vessie et de peau de lapins. Les fibroblastes vésicaux (FV) et dermiques (FD) récoltés produisent et assemblent leur propre matrice extracellulaire (MEC). Les feuillets de cellules et de MEC produits sont ensuite roulés sur un mandrin. Des tests de tension sur anneaux ont permis de connaître l'impact de chaque type cellulaire sur la force tolérée, la déformation des substituts et ainsi d'estimer la pression d'éclatement. Des tests de rétention de sutures sont aussi pratiqués et ce, sur des greffons de 1.5 cm, implantés chez le lapin pour une période de 2 à 6 semaines. Des histologies ont permis de caractériser les tissus produits pré et post-implantation.
Résultats : La construction présente une force de rétention de suture moyenne de 40.18+/-17.7 g/f, qui diffère selon les cellules employées. Les résultats préliminaires montrent qu'il n'y a pas de différence significative entre les propriétés mécaniques des différentes constructions. La pression d'éclatement estimée s'élève en moyenne à 736 mmHg et varie en fonction du nombre de semaines de maturation, tandis que l'urètre natif de lapin peut atteindre un maximum de 45.5mmHg. Des chirurgies exploratoires chez le lapin prouvent la faisabilité de la technique de reconstruction et nous permettent de procéder à des améliorations avant les essaies précliniques. Certaines complications telles que des sténoses sont survenues, mais aucune fistule, ni abcès ont été répertoriées. Après 4 semaines post-implantation, le greffon est complètement recouvert par l'urothélium qui a migré des berges de la plaie pour protéger le tissus reconstruit.

Conclusions : Notre substitut reconstruit par génie tissulaire présente une rétention de suture suffisante pour l'application chirurgicale, ainsi qu'une résistance mécanique au delà de celle du tissus natif. Ces travaux démontrent donc notre capacité à produire un subtitut urétral de lapin autologue qui peut résister aux contraintes physiologiques. Il est prêt à être ensemencé avec des cellules urothéliales avant les études In-vivo à long terme chez le lapin.

Modèle murin du cancer de la prostate : effect d'Ikke et des androgenes sur la croissance tumourale

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Introduction et objectifs : Suite au traitement de déplétion androgénique (TDA), le cancer de la prostate (CaP) peut progresser d'une forme hormono-sensible (HS) vers une résistance à la castration (RC). Notre laboratoire a mis en évidence que l'expression d'IKKε est spécifique aux stades avancés du (CaP). Actuellement, nous étudions l'influence des androgènes sur le rôle d'IKKε dans la progression de la maladie.
Matériels et méthodes : Nous avons injecté dans des souris SCID des cellules 22Rv1 HS du CaP. Celles-ci surexpriment IKKε ou LacZ (contrôle) de façon inductible à la doxycycline (22Rv1-6TR-IKKε et 22Rv1-6TR-LacZ). Nous avons comparé 72 animaux castrés et 72 non castrés, alimentés ou non en doxycycline. Afin d'étudier l'implication du récepteur aux androgènes (RA), nous avons dérivé des clones HS sous-exprimant constitutivement le RA (22Rv1-6TR-IKKε/shAR). Il en est de même avec des clones RC, où la sous-expression d'IKKε est inductible, et où nous avons rétabli l'expression constitutive du RA (PC3-6TR-shIKKε/AR).
Résultats : Tel qu'attendu, en raison de l'hormono-sensibilité des cellules 22Rv1, la croissance des xénogreffes 22Rv1-6TR-LacZ est négativement affectée par la castration mais pas par la doxycycline. En revanche, la croissance des xénogreffes 22Rv1-6TR-IKKε est diminuée lorsque IKKε est exprimée et cet effet est amoindri suite à la castration.
Conclusions : Nos résultats démontrent que la présence d'androgènes concomitante avec l'expression d'IKKε a un effet positif sur la survie des souris injectées avec des cellules HS. La réduction observée de cet effet avec des animaux castrés suggère que l'activité d'IKKε sur la croissance tumourale est contextuelle et influencée par les androgènes. Afin de décrire les mécanismes impliqués, nous souhaitons étudier la prolifération cellulaire, analyser la mort cellulaire, le cycle cellulaire et la sénescence en fonction de la stimulation androgénique. Des xénogreffes avec des clones 22Rv1-6TR-IKKε/shAR seront également réalisées afin de compléter notre étude.

Échec de sonde ureteral double J pour des lithiases obstructives infectées de l'arbre urinaire superior : incidence et facteurs de risqué en Amerique du Nord

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Introduction et objectifs : Déterminer l'incidence et les facteurs de risque associés à un échec de sonde urétérale pour décomprimer une obstruction causée par une urolithiase infectée. Nous avons défini l'échec comme étant la nécessité d'installer une néphrostomie percutanée après installation d'une sonde urétérale.
Matériels et méthodes : En utilisant la banque de données américaine « Nationwide Inpatient Sample » nous avons analysé les tendances temporelles pour déterminer l'incidence d'échec des sondes urétérales pour des urolithiases obstructives. Également, nous avons mesuré le pourcentage de changement annuel estimé (PCAE) entre 1988 et 2010. Une régression logistique a été utilisée pour estimer le Odds Ratio d'avoir un échec de sonde urétérale selon les caractéristiques des patients et du centre hospitalier.
Résultats : Durant la période étudiée, 164,546 doubles J furent installés avec un taux de succès de décompression de 97.8%. Le taux de succès de décompression ainsi que le taux d'échec ont augmentés avec le temps (PCAE 14.05%, p0.001; PCAE 11.61%, p0.001). Les hommes d'âge moyenne avec des lithiases rénales et présentant une insuffisance rénale aiguë avaient un Odds Ratio plus élevé d'avoir un échec du sonde urétérale ($p<0.05$). Des Nephrostomies percutanées post échec de double J ont été effectuées plus fréquemment dans des centres universitaires urbains que dans des centres communautaires (OR 1.98, $p=0.001$; OR 1.83, $p<0.001$)
Conclusions : La décompression de l'arbre urinaire haut obstrué par une lithiase infectée est presque toujours efficace en utilisant une sonde urétérale de type double J. Un échec de sonde urétérale peut toutefois arriver chez une petite proportion des patients qui aura besoin d'une dérivation par nephrostomie percutanée. Les facteurs de risque qui sont associés à un échec de décompression par sonde double J sont: le genre masculin, la localisation de la lithiase et la présence d'une insuffisance rénale. Des néphrostomies percutanées post échec de sonde double J sont faites le plus souvent dans des centres universitaires urbains.

Résultats à long terme de la chirurgie de prolapsus d'organes pelviens utilisant meche trans-vaginale

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Introduction et objectifs : L'utilisation de mèches trans-vaginales synthétiques pour la réduction chirurgicale des prolapsus des organes pelviens (POP) a été démontrée efficace et sécuritaire. Or, le American Food and Drug Association, ainsi que Santé Canada, ont émis des avertissements concernant la sécurité de ces mèches. Notre objectif est de répertorier les résultats cliniques, ainsi que les taux de complications et de récidive de ce type de chirurgie dans notre centre hospitalier.
Matériels et méthodes : Nous avons évalué de façon rétrospective les dossiers de 225 patientes, âgées entre 52 et 96 ans (moyenne 75,6 ans), ayant subi une cure de POP utilisant mèche trans-vaginale dans notre centre, entre 2000 et 2013. 211 (93,7%) patientes souffraient d'un prolapsus de multiples compartiments. 204 (90,7%) des patientes présentaient un prolapsus du compartiment antérieur (cystocèle) dont 68,4% étaient de haut grade (grade ≥ 3), 203 (90,2%) un POP du compartiment moyen (colpocèle ou prolapsus utérin) dont 44,4% de haut grade, et 196 (87,1%) un POP du compartiment postérieur (rectocèle) dont 36,4% de haut grade. 69 (30,7%) patientes avaient un entérocèle associé. Les chirurgies ont toutes été effectuées par le même chirurgien. Le suivi post-opératoire était à 2 mois, 6 mois et ensuite annuellement pour un total de 3 à 5 ans. Nous avons relevé les caractéristiques pré-opératives des patientes, le type de chirurgie, l'examen gynécologique post-opératoire lors du dernier suivi, ainsi que l'évaluation de la satisfaction subjective des patientes (score PGI-I).
Résultats : Le suivi post-opératoire moyen était de 29,2 mois (entre 2 et 130 mois). Sur 225 patientes, 29 (12,9%) ont récidivé de leur prolapsus opéré, dont 16 (7,1%) en étaient symptomatiques et 13 (5,8%) ont du être réopérées. Les taux d'érosion urétrale et d'extrusion vaginale étaient de 0% et 4% respectivement. Il y avait 3 cas rapportés de dyspareunie post-opératoire, et 2 cas de douleur périnéale chronique. Globalement, 161 (71,6%) des patientes se disaient subjectivement très améliorées par la chirurgie (score PGI-I de 1).
Conclusions : L'utilisation de mèches trans-vaginales synthétiques pour la réduction chirurgicale des POP symptomatiques, dans les mains d'un chirurgien entrainé et avec une indication appropriée, est une option chirurgicale efficace et sécuritaire. Les résultats à long terme de cette technique chirurgicale sont excellents, et la satisfaction subjective de la part des patientes est élevée.

Appels sur les gardes dans le programme d'urologie

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Introduction et objectifs : Ce que représente le service de garde assumé par les résidents n'est pas réellement documenté de façon locale ou dans la littérature. Une partie de ce travail passe par la gestion des appels reçus via les téléavertisseurs. Un désir de documenter les caractéristiques des appels reçus, la perception de leur pertinence par les résidents ainsi que

de faire ressortir les éléments évitables a amené ce projet. Un désir de mise à jour et de standardisation du fonctionnement des résidents face aux appels a aussi été pris en compte dans l'élaboration de ce projet.
Matériels et méthodes : Nous avons prospectivement recueilli de l'information sur les appels pendant les gardes de tous les résidents (10) sur des cartons standardisés pendant 2 périodes ciblées de 4 semaines (instigateur et provenance des appels, sujet, action prise, besoin de se déplacer, date, heure, pertinence perçue). Les résidents ont rempli à chaque période un questionnaire pré et post collecte pour évaluer leur perception du nombre et de la pertinence des appels ainsi que leur degré de participation et de motivation au projet.
Résultats : Un total de 460 appels ont été documentés sur 97 jours de garde des deux listes couvertes par les résidents. Il y avait en moyenne/une médiane (étendu) 3,5/3 (0–12) appels par jour de semaine et 7,7/6 (0–23) appels par jour de fin de semaine. Les appels amenaient un déplacement dans 22% des cas (20% pour les jours de semaine et 23,5% pour les jours de fin de semaine). Les appels après 23h00 représentaient 13% des appels reçus (18% la semaine, 7% la fin de semaine). La plupart des appels (75%) étaient perçus comme pertinents ou très pertinents. Les appels provenaient des infirmières dans 66% des cas, des commis dans 4%, d'autres médecins dans 22%, de pharmaciens dans 4%, des téléphonistes dans 1% et d'autres /pas d'information dans 3%. L'étude du contenu des appels est en cours. Dans les questionnaires post collecte, tous les résidents sauf 1 à une période ont indiqué avoir documenté au moins 80% des appels reçus.
Conclusions : Nous avons maintenant un bilan plus objectif de ce que représente le travail des résidents du programme d'urologie pendant leurs gardes. Il est difficile de comparer avec d'autres programmes ou d'autres milieux de formation étant donné que c'est la seule étude à notre connaissance à ce sujet. À noter que ce bilan demeure une sous-estimation du travail réel.

Short-term outcome of metastasectomy in renal cell carcinoma: The Canadian Kidney Cancer Information System initial experience

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Introduction et objectifs : Metastatic renal cell carcinoma (RCC) remains associated with a high mortality rate. Metastasectomy (M) is an acceptable treatment option for selected patients. Our aim was to evaluate the effect of surgical resection (SR) of metastasis on disease recurrence and survival.
Matériels et méthodes : Using the Canadian Kidney Cancer Information System (CKCis), we identified patients who underwent surgical resection of metastatic Renal Cell Carcinoma (mRCC). We evaluated the histological features of the primary renal cancer, the sites of metastasis and whether M was complete or incomplete. The use of systemic therapy (ST) before or after M and its impact on the outcome of SR was evaluated. Kaplan Meier analysis was performed to assess the metastasis-free survival (MFS) and overall survival (OS) for patients who underwent complete or incomplete SR. Statistical analysis was performed using R.
Résultats : At the time of this analysis 784 patients with mRCC were present in the CKCis database. Of those, 124 patients underwent SR of their mRCC. Median age at the time of M was 60 (IQR 53 – 66). The mean time between diagnosis of RCC and mRCC was 1.87 (IQR 0 – 2.33) years. The median follow-up duration was 1.5 (IQR 0.7–3.35) years. The majority of our patients (73%) had clear cell carcinoma histology. The most common site of M was lung, bone, adrenal, brain and liver in 41 (33%), 20 (16%), 11 (9%), 9 (7%) and 9 (7%) patients respectively. Fifteen (12%) patients had ST before, 59 (48%) after surgery, and 50 (40%) did not receive any ST. Seventy (56%) patient had complete resection of all visible disease (sNED),38 (31%) had incomplete resection and 16 (13%) patients had unknown resection status. Complete SR was achieved in 10 (67%) patients who had initial ST and in 60 (55%) patients with no prior ST. Fifty-seven patients developed a new site of metastasis during follow-up, 53% with incomplete resection and 53% with complete resection. At the time of the last follow-up, 29 (23%) patients were alive with no evidence of disease, 73 (59%) patients were alive with disease, 15 (12%) patients died of disease and 7 (6%) patients were lost to follow-up.
Conclusions : In the absence of curative medical treatments, surgery should remain a valid option for patients with limited metastatic burden. A larger cohort and longer follow-up will be needed to identify ideal patients and sequence of treatment.

Immediate focal therapy vs. active surveillance of localized low-intermediate risk prostate cancer

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Introduction et objectifs : Active surveillance (AS) is commonly recommended for men with localized low-intermediate risk prostate cancer (PCa) apparently confined to one side of the prostate. Focal therapy may be considered for selected cases and it is still under investigations. Our aim is to assess the probability of developing unfavorable disease features (UDF) while under AS as a guide to whether instituting immediate rather than delayed hemiablation therapy (HAT) is appropriate.
Matériels et méthodes : Of the 300 patients diagnosed with adenocarcinoma of the prostate between 1992 and 2012 who either elected to be managed by AS or refused treatment, 157 had biopsy proven unilateral prostate cancer at diagnosis. Patients were followed every 3–6 months with prostate-specific antigen (PSA) and physical examination and were offered repeat ultrasound-guided systematic 6–16 cores biopsies every 1–3 years. Using five different definitions of UDF, patients' data were used to simulate the theoretical outcome if all patients were managed by immediate HAT or AS. Kaplan-Meier curves were used to evaluate the probability of developing UDF while on AS, or following immediate HAT.
Résultats : The mean age at the time of diagnosis was 67 years (range 47–81). The median was 5.4 (IQR range 3.4–8) years. Eighty-three (53%) patients had >1 repeat biopsy. Baseline characteristics included a median (IQR): PSA of 5.5ng/ml (4.5–7), number of biopsy cores taken of 10 (6–10), maximum cancer percentage on any core of 10 (5–20), and number of patient (%): 144 (92) with a Gleason score (GS) >6. By using the most strict to least strict definition of UFD, 10 to 47% patients that would develop UDF while under AS, respectively. While comparing the baseline GS, maximum cancer percentage and PSA density (PSAd), we found a significant trends for higher development of UFD during AS.
Conclusions : Many men did not develop UDF during AS follow-up, and thus could be spared the negative consequences of immediate HAT.

Programme Scientifique – Session IV
Vendredi 7 novembre 2014

Assessing the impact of recent modifications in the management of urinary tract infection on the severity of disease in children with vesicoureteral reflux undergoing ureteral reimplantation

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Introduction et objectifs : The release of clinical practice guidelines in 1999 by the American Academy of Pediatrics on the diagnosis, treatment, and evaluation of initial urinary tract infections (UTIs) in febrile infants and young children, further revised in 2011, led to significant practice changes in Pediatrics. Accordingly, our institution published in February 2012 an adapted plan for the management of UTIs. Such changes inevitably led to subsequent modifications in diagnosis and management of children with vesicoureteral reflux (VUR) associated UTIs. For those children especially, secondary renal damage remains of concern. Therefore, the aim of this study is to evaluate whether changes in local pediatric practices led to an increase in renal scarring among patients requiring surgical care.
Matériels et méthodes : Between 2005 and 2013, 300 surgeries were performed at our institution for children with primary VUR (110 cases of ureteral reimplantations; 41 unilateral vs. 69 bilateral). Ureters operated prior to (group 1; n=137) and after (group 2; n=42) February 2012 were compared in terms of VUR grade, kidney bipolar size standardized for age, and renal scaring.
Résultats : The median age was 2.3 (1.7–4.4) years old, 58.2% patients underwent bilateral surgery and 7.9% of ureters had a duplex collecting system. Groups 1 and 2 were similar for all three variables, and for both the median VUR grades (3.0 vs 4.0, p=0.447) and the kidney bipolar size (7.0 vs 7.4 cm, p=0.145). However, group 1 had a lower proportion of kidneys with >2 scars (27.3% vs 51.3%, p=0.007) and of diffuse renal damage (8.5% vs 21.6%, p=0.031). Additionally, group 2 was associated with a two-fold increased risk of kidney scaring (CI95%: 1.007–4.774, p=0.048). The median age was 2.3 (1.7–4.4) years old, 58.2% patients underwent bilateral surgery and 7.9% of ureters had a duplex collecting system. Groups 1 and 2 were similar for all three variables, and for both the median VUR grades (3.0 vs 4.0, p=0.447) and the kidney bipolar size (7.0 vs 7.4 cm, p=0.145). However, group 1 had a lower proportion of kidneys with >2 scars (27.3% vs 51.3%, p=0.007) and of diffuse renal damage (8.5% vs 21.6%, p=0.031). Additionally, group 2 was associated with a two-fold increased risk of kidney scaring (CI95%: 1.007–4.774, p=0.048).
Conclusions : Although cohorts are unpredictably similar, results show that patients operated after the changes in management recommendations for UTI-associated VUR have increased renal scarring. Consequently, physicians should take into account the risks associated with conservative management of UTI in children.

Endoscopic treatment with dextranomer/hyaluronic acid copolymer (Deflux) vs. ureteral reimplantation in the management of children with vesicoureteral reflux (VUR): An overview of the surgical management observed over time at a teaching institution

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Introduction et objectifs : Guidelines for the diagnosis and management of urinary tract infections (UTIs) in infants and young children published in recent years did not necessarily help clarify how to care for patients later diagnosed with VUR. To prevent the complications associated with UTIs in such cases, the surgical management usually either consists of an endoscopic treatment or a ureteral reimplantation. A previous report from our institution showed comparable but disappointing success rates of Deflux injections during the 2005 to 2008 period. A part two analysis aimed to evaluate our change in practice during the 2009 to 2012 period, and showed a decrease in the number of endoscopic procedures performed and an increase in the volume injected, with no change in outcome. Thus, we now aim to assess how our practice changed accordingly.
Matériels et méthodes : This single-institution cohort is composed of patients diagnosed with VUR whom underwent ureteral reimplantation or Deflux injections in 2005–2008 (group 1, n=153) and 2009–2012 (group 2, n=121). Patients with prior history of VUR surgery were excluded. A multivariate analysis was performed to evaluate which variables influenced the choice of surgery during both periods.
Résultats : Both groups were similar in terms of gender (males: 37.3% vs. 38%, p=0.897), bilateral interventions (56.9% vs. 53.7%, p=0.687), and age (4.8 y.o. (2.1–7.5) vs. 3.7 y.o. (2.0–6.7), p=0.102). The proportion of reimplantations performed over endoscopic treatment increased from group 1 to group 2 (p<0.001). In fact, prior to 2009, 25.4% of refluxing ureters (62/244 ureters) were corrected with reimplantation, especially in younger patients (OR=0.835, p=0.021) with higher grade VUR (OR=1.705, p=0.007). After 2009, 50.5% (96/290 ureters) had ureteral reimplantations. The choice was most influenced by male gender (OR=3.395, p=0.001), a younger age (OR=0.711, p<0.001) and kidney scarring (OR: 2.248, p=0.044).
Conclusions : While both cohorts are unpredictably very similar, the proportion of ureteral reimplantation performed over endoscopic treatment using Deflux injections has increased after 2009. Therefore, assessing the disappointing success rate of Deflux injections in our teaching institution seems to have favored the choice for ureteral reimplantation.

L'utilisation du mirabegron dans le traitement de la vessie hyperactive en pédiatrie : une nouvelle option thérapeutique

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Introduction et objectifs : Les urologues pédiatriques sont souvent confrontés aux symptômes de la vessie hyperactive. Actuellement, les anticholinergiques constituent le traitement de choix de cette condition, mais plusieurs effets secondaires sont rapportés. Le développement d'une nouvelle thérapie pharmacologique avec un mécanisme d'action différent serait donc souhaitable. Récemment, un agoniste b3-adrénergique, soit le Mirabegron, a été développé pour le traitement de la vessie hyperactive. Les études ont démontré une amélioration significative des symptômes et peu d'effets secondaires ont été décrits. L'efficacité demeure par contre inconnue chez la population pédiatrique. L'objectif de notre étude est d'évaluer l'efficacité et la tolérabilité du Mirabegron chez les patients pédiatriques ayant une vessie hyperactive réfractaire au traitement anticholinergique.
Matériels et méthodes : Une étude prospective utilisant des doses ajustées de Mirabegron (25 à 50 mg) a été conduite chez les patients pédiatriques.

Les patients ayant été traités avec une thérapie comportementale intensive et au moins 2 anticholinergiques différents et qui n'ont pas répondu au traitement et/ou ont présenté plusieurs effets secondaires ont été inclus dans l'étude. L'efficacité et la tolérabilité ont été mesurées par des calendriers mictionnels, des résidus post-mictionnels, des cultures d'urine, un ECG, des signes vitaux et un bilan urodynamique si jugé nécessaire. Les familles ont été questionnées sur la continence, la compliance et les effets secondaires. L'efficacité a également été évaluée à l'aide de l'échelle de perception de la condition vésicale (PPBC).
Résultats : Vingt-six patients avec vessie hyperactive ont été enrôlés. L'âge moyen au début du traitement était de 126 mois et les patients ont été traités avec Mirabegron un minimum de 3 mois. La capacité vésicale moyenne a été majorée suite au traitement, passant de 181 ml à 253 ml. Jusqu'à maintenant, la continence s'est améliorée chez tous les patients, à l'exception d'un, et 4 sont maintenant complètement secs. Suite au traitement, les résidus post-mictionnels chez la totalité des patients se sont avérés non significatifs (<20ml). Le PPBC moyen s'est amélioré de 4,4 à 2,2. Quatre patients ont rapportés des effets secondaires légers à modérés. Les effets secondaires rapportés étaient la rhinite, les crampes abdominales, la constipation et les nausées. Les ECG et les signes vitaux sont tous restés inchangés.
Conclusions : L'utilisation du Mirabegron, un nouvel agoniste b3-adrénergique, peut améliorer de façon notable les symptômes de la vessie hyperactive réfractaire en pédiatrie. Le traitement a été bien toléré dans cette première étude menée en pédiatrie.

Développement d'un modèle tridimensional in vitro issue du génie tissulaire pour l'étude du cancer de la vessie

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Introduction et objectifs : Le cancer de la vessie est le cinquième cancer le plus diagnostiqué au Canada. À ce jour, il n'existe que peu de modèles in vivo ou in vitro permettant l'étude des mécanismes de progression de cellules urothéliales cancéreuses dans leur environnement physiologique. Notre équipe possède une expertise unique dans le développement d'équivalents vésicaux entièrement humains reconstruits par génie tissulaire. Le but de cette étude est de développer un modèle à l'aide de ces équivalents sur lesquels nous ferons croitre des tumeurs urothéliales ce qui nous permettra d'étudier les mécanismes de progression du cancer vésical.
Matériels et méthodes : Des fibroblastes dermiques sont cultivés avec du milieu contenant du sérum et de l'acide ascorbique permettant la formation de feuillets matriciels. Suite à la superposition de trois feuillets, des cellules urothéliales sont ensemencées sur ces constructions. Après la maturation de l'urothélium en interface air-liquide, des microsphères de différentes lignées urothéliales cancéreuses sont implantées dans l'urothélium en prenant soin de ne pas transgresser la lame basale. Nous y avons laissé croitre ces sphéroïdes pendant sept et quatorze jours. Finalement, les équivalents ont été biopsiés et analysés par histologie et par immunohistochimie.
Résultats : Toutes les lignées cancéreuses testées on été en mesure de croitre sur les équivalents vésicaux et ce de façon reproductible. Le comportement des tumeurs ainsi formées était variable selon la nature des cellules utilisées. Les lignées non invasives étaient incapables de traverser la lame basale contrairement aux lignées invasives qui elles, le pouvaient.
Conclusions : Par ces expériences, nous avons démontré qu'il est possible de produire un modèle 3-D in vitro de cancer de vessie sur un équivalent vésical reconstruit pas génie tissulaire. Ce modèle ouvre la porte à un nouveau mode d'étude des divers mécanismes de progression du cancer de la vessie et ce dans un contexte plus physiologique que les modèles existants. À terme, il pourrait permettre d'identifier de nouvelles cibles thérapeutiques et de développer de nouveaux traitements individualisés contre le cancer de la vessie.

Prevalence and risk factors of contralateral extraprostatic extension in men undergoing radical prostatectomy for localized unilateral disease at biopsy: A global multi-institutional experience

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Introduction et objectifs : Interfascial nerve-sparing technique during robotic-assisted radical prostatectomy (RARP) may be performed on the contralateral side of unilaterally diagnosed prostate cancer (PCa). Unsuspected bilateral disease could be associated with extraprostatic extension. We aim to assess the incidence and risk factors of contralateral EPE (cEPE) and contralateral positive surgical margins (cPSM) in patients diagnosed preoperatively with unilateral disease. Interfascial nerve-sparing technique during robotic-assisted radical prostatectomy (RARP) may be performed on the contralateral side of unilaterally diagnosed prostate cancer (PCa). Unsuspected bilateral disease could be associated with extraprostatic extension. We aim to assess the incidence and risk factors of contralateral EPE (cEPE) and contralateral positive surgical margins (cPSM) in patients diagnosed preoperatively with unilateral disease.
Matériels et méthodes : This multicentre cohort consisted of 331 men diagnosed with unilateral PCa who underwent RARP. Localization and occurrence of positive cores from biopsy, cEPE, cPSM and seminal vesicle invasion (SVI) was noted. cEPE+ and cEPE- groups were compared for preoperative predictive parameters.
Résultats : Pathology reported cPCa in 50.2% and cEPE in 4% of the cohort. In patients with bilateral PCa, the cPSM rate of cEPE+ and cEPE- groups was not significantly different (23% vs 10.5%, p=0.170), but the incidence of SVI was significantly increased in the cEPE+ group (38.5% vs 5%, p<0.001). PSA levels of cEPE+ and cEPE- patients was 6.4 µg/L (5.1–14.6) and 5.2 µg/L (4.0–7.1) respectively (p=0.026). The proportion of positive cores, maximum cancer involvement in a core, clinical stage, Gleason score and TRUS size were not significantly different. Lastly, in the pT3 subgroup, the frequency of positive biopsies at the apex increased with contralateral cancer invasion (p=0.007).
Conclusions : Despite the 50% chance of bilateral disease, the risk of cPSM associated with cEPE is only 1% in the cohort. Contralateral nerve-sparing procedures may be considered safe in patients with unilateral disease on preoperative biopsies, especially when associated with a low PSA and negative biopsies at the apex.

Expression of prognostic marker IL-6 in prostate cancer tissue and blood plasma

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Introduction et objectifs : In prostate cancer (PCa) patients, it is established that high serum levels of IL-6 correlate with disease progression, and that IL-6 expressed by PCa cells could reactivate the androgen receptor and stimulate proliferative and anti-apoptotic pathways. Similarly, the expression of the cytoplasmic protein kinase IKKε has been correlated with PCa progression, and associated in vitro with an increase in the secretion of IL-6. To further our understanding of IL6's role in PCa, we aim to evaluate the relationship between IL-6 tissue expression and serum levels in advanced disease. As a secondary endpoint, we aim to correlate in tissu expression of IKKε and IL-6.
Matériels et méthodes : Immunofluorescent co-staining of IKKε and IL-6 was performed using large-scale PCa tissue microarrays (TMA), composed of samples of various tumour grades (n=230). Signal quantification was performed using the VisiomorphTM image analysis platform. Cytokine

serum levels were measured by ELISA assay. Patients were grouped according to the Gleason score of the radical prostatectomy specimen (≤3+3, 3+4, 4+3, ≥4+4).
Immunofluorescent co-staining of IKKε and IL-6 was performed using large-scale PCa tissue microarrays (TMA), composed of samples of various tumour grades (n=230). Signal quantification was performed using the VisiomorphTM image analysis platform. Cytokine serum levels were measured by ELISA assay. Patients were grouped according to the Gleason score of the radical prostatectomy specimen (≤3+3, 3+4, 4+3, ≥4+4).
Résultats : ELISA assay analysis indicated that patients had respectively lower IL-6 serum levels as tumour grade increased. In the low grade disease group (≤3+3), patients with IL-6 serum levels above 8.5 pg/ml tended to have a higher risk of biochemical recurrence (BCR) than their respective counterparts (p=0.088). Furthermore, every 1 pg/ml increase in IL-6 serum levels was associated with a 2.4% increased risk of BCR (CI 95%: 1.009–1.038, p=0.001) in patients with Gleason scores ≤3+3. Immunofluorescent co-staining of IL-6 and IKKε has been optimized on TMA test samples. An additional staining targeting epithelium-specific protein (PSA, cytokeratin 18 and 19) has been developed to quantify IL-6 and IKKε in tissu levels to the epithelium restrictively. ELISA assay analysis indicated that patients had respectively lower IL-6 serum levels as tumour grade increased. In the low grade disease group (≤3+3), patients with IL-6 serum levels above 8.5 pg/ml tended to have a higher risk of biochemical recurrence (BCR) than their respective counterparts (p=0.088). Furthermore, every 1 pg/ml increase in IL-6 serum levels was associated with a 2.4% increased risk of BCR (CI 95%: 1.009–1.038, p=0.001) in patients with Gleason scores ≤3+3. Immunofluorescent co-staining of IL-6 and IKKε has been optimized on TMA test samples. An additional staining targeting epithelium-specific protein (PSA, cytokeratin 18 and 19) has been developed to quantify IL-6 and IKKε in tissu levels to the epithelium restrictively.
Conclusions : Preliminary results demonstrate that high IL-6 serum levels in patients with low grade PCa could help identify patients with a higher risk of BCR. To validate these results on a larger cohort, this analysis will be extended on serum samples of 600 patients. Further analysis will give additional insight on the relation between IL-6 serum and in tissu levels and help evaluate whether IKKε expression could be combined to IL-6 serum levels as a prognostic tool for PCa. Preliminary results demonstrate that high IL-6 serum levels in patients with low grade PCa could help identify patients with a higher risk of BCR. To validate these results on a larger cohort, this analysis will be extended on serum samples of 600 patients. Further analysis will give additional insight on the relation between IL-6 serum and in tissue levels and help evaluate whether IKKε expression could be combined to IL-6 serum levels as a prognostic tool for PCa.

Infected urolithiasis among patients with inflammatory bowel disease: A review of US emergency department visits between 2006 and 2009

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Introduction et objectifs : Patients with inflammatory bowel disease (IBD) are at risk of developing urolithiasis as well as infections. However, studies investigating IBD patients with infected urolithiasis are limited. Using population-based data, we hypothesized that IBD patients with infected urolithiasis present more frequently to emergency departments (ED) and with more severe infections.
Matériels et méthodes : Using the Nationwide Emergency Department Sample (NEDS), we identified all patients presenting to U.S. EDs with diagnoses of urolithiasis. We then extracted a subgroup with concomitant diagnosis of IBD. We compared rates of urinary tract infection (UTI), sepsis, organ failure, hospitalization and mortality between the two groups. Using multivariate analysis we determined whether or not IBD was a predictor of UTI, sepsis and hospitalization.
Résultats : IBD patients with urolithiasis presented with infections (8.1 v 10.4%, p<0.001), sepsis (0.2 v 0.6%, p<0.001) and end-organ failure (1.6 v 6.3%, p<0.001) more frequently than non-IBD patients. They were also more likely to have characteristics independently associated with infection and sepsis, such as older age and female gender. In adjusted analyses, a diagnosis of IBD was an independent predictor of infection (OR 1.3 [1.135 – 1.455], p<0.0001), sepsis (OR1.8 [1.095 – 2.919], p<0.0001) and admission (OR3.3 [3.04 – 3.635], p<0.0001).
Conclusions : IBD patients with urinary stone disease require emergency care more commonly for associated UTI, renal failure and sepsis than the general stone population. Given the increased frequency and severity of complicated stone disease in these patients, preventative measures are warranted.

Programme Scientifique – Session VIII
Samedi 8 novembre 2014

Clinical management and burden of prostate cancer: A markov monte carlo model

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Introduction et objectifs : Background: Prostate cancer (PCa) is the most common non-skin cancer among men in developed countries. Several novel treatments have been adopted by healthcare systems to manage PCa. Observational and trial based studies on effectiveness often evaluated fewer treatments over limited follow-up. A contemporary decision analytic model was necessary to address these limitations by synthesizing the evidence on several treatments thereby forecasting short and long-term clinical outcomes. The objectives of this study were to develop and validate a Markov Monte Carlo model for the contemporary clinical management of PCa; and to assess the clinical burden of the disease from diagnosis to end-of-life.
Matériels et méthodes : A decision model was developed to simulate the management of PCa from diagnosis to end-of-life. Health states modeled were: risk at diagnosis, active surveillance (AS), initial treatments (radical prostatectomy or radiation therapy), PCa recurrence, PCa recurrence free, metastatic castrate resistant prostate cancer (mCRPC) and death (cause specific/other causes). Treatment trajectories were based on state transition probabilities derived from the literature. Validation and sensitivity analyses assessed the accuracy and robustness of model predicted outcomes.
Résultats : Validation demonstrated good agreement between model predicted outcomes and observed outcomes. Over the lifetime simulated period 21.6% died from PCa and 78.4% died from other causes. Over lifetime for low-, intermediate-, high- risk groups the PCa and overall death rates were 4.2%, 15.7%, 34.6% and 95.8%, 84.3%, 65.4%; respectively.
Conclusions : The model predicted rates were corroborated by the observed rates in the literature. This model could be used to assess healthcare resource use and costs associated with PCa treatments.

High hospital and surgeon volume and its impact on overall survival after radical cystectomy among patients with bladder cancer in Quebec

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Introduction et objectifs : Previous studies reported improved outcomes for bladder cancer patients who had radical cystectomy (RC) performed by surgeons and hospitals with high annual RC volumes. The objective of this study was to determine the effect of high hospital and surgeon volume on survival after RC for bladder cancer in Quebec.
Matériels et méthodes : We conducted a retrospective cohort study using data of patients who underwent RC for bladder cancer from 2000 to 2009. The cohort was obtained with the linkage of two health databases: the RAMQ database (data on medical services), and the ISQ database (demographic data on births and deaths). We excluded patients who did not survive within the first 30 days after RC. Hospital volume was defined as the average annual number of RC performed at an institution during the study period. Surgeon volume was defined as the average annual number of RC performed by a surgeon during his active years. We considered high hospital and surgeon volume those hospitals and surgeons falling in the 3rd or 4th quartile of the distribution of hospital and surgeon volumes. The effect of high hospital and surgeon volume on survival was assessed by multivariate Cox proportional hazards models.
Résultats : We analyzed a total of 2700 patients who met inclusion criteria (75% males). The average annual RC hospital volumes in the 3rd and 4th quartiles were 17.5 and 36, respectively. Average annual RC surgeon volumes in the 3rd and 4th quartiles were 3.4 and 8.9. High hospital volume was found to be significantly associated with improved survival (HR=0.82, 95% CI: 0.71–0.95). Moreover, patients who had their RC performed in a high volume hospital and by a high volume surgeon had a 13% decreased risk of mortality compared with other patients (HR=0.87, 95%CI: 0.77–0.99).
Conclusions : Having RC for bladder cancer performed by high volume surgeons in high volume hospitals was associated with improved overall survival compared with low volume providers.

Laparoscopic extravesical ureteral reimplantation: Refinement of the technique

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Introduction et objectifs : Our current technique of laparoscopic ureteral reimplantation has evolved with the addition of 3 dimensional (3D) vision endoscopy, bipolar cautery and a 3 port approach. We evaluated the benefit of the current 3D technique by comparing it to a previous cohort of 2 dimensional (2D) laparoscopy.
Matériels et méthodes : Charts of 19 consecutive children who underwent laparoscopic extravesical ureteral reimplantation by a single surgeon from 2005 to 2013 for vesicoureteral reflux (VUR) were retrospectively reviewed. The current 3D (11 patients) cohort was compared to the previous 2D (8 patients) cohort, excluding cases from 2002–2005 to account for the learning curve. Data on age, weight, gender, grade of VUR, dimension, technique of detrusor tunnel mucosal dissection, tunnel length, operative time, length of stay, and complications were retrieved. All statistical analysis was conducted per ureter (total of 28 ureters operated). Statistical tests included linear regression models and chi squared tests for trend, conducted using STATA software.
Résultats : The median age of all patients was 5yrs, with the distribution of grades of VUR from 1 to 5 being 1-9-8-10-0, with 4 cases of common sheath reimplantation. The mean operative time for 2D (12 ureters) and 3D (16 ureters) was 217min and 130min. When comparing 3D versus 2D laparoscopy, operative time was reduced by an average of 86 minutes per ureter with the use of 3D laparoscopy ($p<0.0001$), and mucosal perforation rate was decreased from 67% to 19% ($p=0.01$). Operative time increased by a mean of 72 minutes when a perforation occurred ($p=0.005$). There was no statistically significant difference between the 2 groups in the number of bilateral cases, median age or weight, mean detrusor tunnel length, nor grade of reflux. The 3D group was different in that the bipolar hook was used in 7 cases and 3 ports were used instead of 4. The use of 3D laparos-

copy did not significantly impact the length of hospital stay.
Conclusions : Operative times and mucosal perforation rates are significantly reduced with the use of 3D vision endoscopy and the bipolar hook for extravesical ureteral reimplantation, compared to conventional laparosocopy with right angle monopolar electrocautery. The 3D approach provides a novel alternative to which robotic assisted techniques should be more critically evaluated.

Laparoscopic pyeloplasty: Impact of 3D vision laparoscopy and articulating shears

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Introduction et objectifs : To compare outcomes of laparoscopic pyeloplasty in a cohort of children with 3 dimensional (3D) vision laparoscopy and articulating shears to a cohort with standard 2 dimensional (2D) laparoscopy.
Matériels et méthodes : Medical charts of 33 consecutive patients with ureteropelvic junction obstruction who underwent laparoscopic pyeloplasty by a single surgoen from 2006 to 2013 were reviewed in a retrospective manner. The current 3D cohort was compared to the previous 2D cohort, excluding cases from 2001–2005 to account for the learning curve. Excluded from the study were 3 cases of prior pyeloplasty, 2 because of ureteroscopy for fibroepithelial polyps and 1 open conversion in a duplex kidney with intrarenal pelvis. Data on age, weight, gender, side, operative time, dimension (2D=19 patients, 3D=8 patients), presence of a crossing vessel, length of hospital stay and complication rate were compared between the two groups. Articulating shears were used for pelvotomy and spatulation of the ureter. Statistical tests included linear regression models and chi square tests for trend using STATA software.
Résultats : The median age and weight of the population was 7.5 yrs and 28.5kg, and 19 out of 27 patients had a crossing vessel. Operative time per case was decreased by an average of 48 minutes in the group undergoing 3D laparoscopic surgery compared to the group undergoing 2D laparoscopic surgery (p=0.02). When adjusted for the presence of a crossing vessel, operative time was still significantly shorter in the 3D group (p=0.03). There was no difference in median age, weight, or presence of crossing vessel between both groups. Complication rate and length of hospital stay were not significantly affected by the use of 3D laparoscopy. The majority (7 out of 8) of 3D cases where performed using the laparoscopic flexible scissors, which was significantly associated with operative time (p=0.02).
Conclusions : The use of 3D vision laparoscopy and articulating shears for pyeloplasty in children appears to significantly reduce the operative time compared to conventional 2D laparoscopy with rigid scissors. This approach provides a hybrid alternative to current robotic assisted technology, and deserves further attention in view of the significant cost savings.

Implication du facteur de transcription E2F3 dans la surexpression de PACE4, dans le cancer de la prostate

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Introduction et objectifs : La proprotéine convertase PACE4 est une enzyme qui est surexprimée dans les cellules néoplasiques de la prostate. Son inhibition dans des modèles cellulaires de cancer de la prostate permet d'inhiber la prolifération de ces cellules, faisant de la PACE4 une cible thérapeutique intéressante pour le développement de nouveaux agents anti-néoplasiques. L'implication du gène E2F3 dans le cancer de la prostate a déjà été démontrée dans la littérature, et des études sur biobanques dans notre centre ont révélé une corrélation entre l'expression de E2F3 et les niveaux de PACE4. Notre visée est de valider au niveau moléculaire cette corrélation.
Matériels et méthodes : Nous avons transfecté de l'ARN interférant (siRNA) dans une lignée cellulaire (HT1080) surexprimant la PACE4, pour y réduire l'expression de E2F3. L'efficacité du knockdown, ainsi que la subséquente réduction d'expression de PACE4, ont été ensuite mesurés par PCR quantitative (qPCR).
Résultats : Suite à une transfection adéquate de siRNA, nous avons réussi à démontrer une réduction de plus de 80% de l'expression de E2F3 dans la lignée cellulaire étudiée. Il s'en suit une réduction de près de 40% de l'expression de PACE4 dans ces mêmes cellules.
Conclusions : Nos expériences appuient la corrélation E2F3-PACE4. Le gène E2F3 pourrait s'agir d'un facteur de transcription, parmi d'autres, permettant la surexpression de PACE4 dans le cancer de la prostate.

The use of GreenLight-SIM simulator during urology objective structured clinical examinations

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Introduction et objectifs : To evaluate the utility of the GreenLight-SIM™ (GL-SIM) simulator to asses Photoselective Vaporization of the Prostate (PVP) skills of urology postgraduate trainees (PGTs) during Objective Structured Clinical Examinations (OSCEs).
Matériels et méthodes : After obtaining ethics approval, PGTs in Post-Graduate Years (PGY-3 to PGY-5) from all four Quebec urology training programs were recruited during two annual OSCEs. During a 20-minute OSCE station, PGTs were asked to perform two exercises: identification of endoscopic landmarks and PVP of a 30 g normal prostate. Grams vaporized, global scores and number of correct anatomical landmarks were recorded and correlated with PGY level, practice on the GL-SIM and previous PVP experience.
Résultats : 25 PGTs were recruited at each OSCE with 13 PGTs participating in both OSCEs. When comparing scores from the 1st to the 2nd OSCE, there was a significant improvement in the number of grams vaporized (2.9 vs. 4.3g; p=0.003) and global score (100 vs. 165; p=0.03). There was good correlation between the number of previously performed PVPs and the global score (r=0.4, p=0.04). Similarly, PGTs with previous practice on the GL-SIM had significantly higher global score (100.6 vs. 162.6; p=0.04) and grams vaporized (3.1 vs 4.1g; p=0.04) when compared with those who did not practice on GL-SIM. PGY level did not significantly affect grams vaporized and global score (p>0.05).
Conclusions : Performance on the GreenLight-SIM at OSCEs significantly correlated with previous practice on the GL-SIM simulator and previous PVP experience rather than PGY level.

Résultats oncologiques et fonctionnels de plus de 700 cas de prostatectomie radicale assistée par robot (PRAR) – plus grande experience canadienne réalisée sur 7 ans

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Introduction et objectifs : La prostatectomie radicale assistée par robot (PRAR) est de plus en plus pratiquée aux Etats-Unis et au Canda dans le traitement du cancer localisé de la prostate. À ce jour, peu d'équipes canadiennes ont publié leurs résultats oncologiques et fonctionnels de l'intervention. Nous présentons ici la plus grande expérience de cas de PRAR pratiquées au Canada.
Matériels et méthodes : Les données de 722 patients ayant subi une PRAR, pratiquées par 4 chirurgiens spécialisés, ont été colligées prospectivement d'Octobre 2006 à Décembre 2013. Les caractéristiques préopératoires, ainsi que les résultats chirurgicaux et pathologiques posto-

pératoires ont été colligés. Les résultats fonctionnels et oncologiques ont aussi été évalués jusqu'à 72 mois après l'opération.
Résultats : Le suivi médian (Écart Interquartile) est de 18 mois (9–36). La répartition du risque de d'Amico est : faible à 31%, intermédiaire à 58% et élevée à 11%. La durée médiane de l'opération est de 178 min (142–205), les pertes sanguines de 200mL (150–300) et une durée d'hospitalisation postopératoire (écart) de 1 jour (1–23). Le taux de transfusion est de seulement 0.7%. On dénombre 0.7% de complications postopératoires majeures (Clavien III-IV) et 10.4% de complications mineures (Clavien I-II), avec aucune mortalité. D'un point de vue pathologique, 445 hommes (70%) sont classifiés stade 2, dont 81 (18%) avec une marge chirurgicale positive. 189 hommes (30%) sont classifiés stade 3, dont 87 (46%) avec une marge chirurgicale positive. Le retour de la fonction urinaire (0 serviette ou couche par jour) à 3, 6 et 12 mois postopératoire est respectivement de 68%, 80% et 90%. La fonction érectile (pénétration possible) pour tous les hommes étudiés à 6, 12 et 24 mois postopératoire était respectivement de 37%, 52% et 59%. Une récidive biochimique a été observée dans 28 cas (4.9%), et 14 patients (2.4%) ont reçu une radiothérapie prophylactique. Au total, 49 patients (8.4%) ont subi une radiothérapie ou/et une thérapie hormonale.
Conclusions : Cette étude montre des résultats semblables à ceux d'autres programmes à volume élevé de PRAR. Étant la plus grande expérience de PRAR réalisée au Canada, nous rapportons que la PRAR est sécuritaire et donne des résultats oncologiques et fonctionnels acceptables dans le cadre canadien.

Survival after radical cystectomy for bladder cancer in relation to prior non-muscle invasive disease in Quebec

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Introduction et objectifs : Radical cystectomy (RC) is indicated in patients with muscle-invasive bladder cancer. However, there is controversy regarding outcomes after RC when examined in relation to prior non-muscle-invasive disease (NMIBC) versus invasive cancer de novo at time of diagnosis. The aim of this study was to determine if there is a difference in survival after RC among the two groups.
Matériels et méthodes : We conducted a retrospective cohort study of all patients who underwent RC in Quebec during the years (2000–2009). The cohort was obtained by the linkage of two administrative databases: the RAMQ database (Quebec health insurance medical services) and the ISQ database (vital status data). We excluded patients with history of neo-adjuvant treatment. Patients were considered as having NMIBC progressing to invasive disease if they had at least 2 trans-urethral resection of bladder tumour (TURBT) held more than 4 months apart before RC. Survival outcomes were compared by hazard ratios generated by Cox proportional hazards models adjusted for age and gender.
Résultats : A total of 2671 subjects who underwent RC met the eligibility criteria, their RCs were performed in 48 hospitals by 122 urologists across Quebec. Among them, 19.8% had prior NMIBC that further progressed to invasive disease, and 80.2% presented with invasive disease de novo. Of the cohort, 69.2% had 1 TURBT, 16.6% had 2 TURBTs and 14.2% had 3 or more TURBTs prior to RC. No significant difference was observed in medical oncology referral for adjuvant treatment among patients with non-invasive and invasive disease (36.9% and 39% respectively, p=0.3). Median survival after RC for patients with prior NMIBC was 4.3 years as compared to patients with invasive disease de novo 3.7 years. (p=0.007, Wilcoxon test). Patients with NMIBC at the time of diagnosis had a 16% decrease in the risk of mortality after RC, when compared to patients with invasive disease de novo (HR=0.84, 95% CI 0.73–0.96).
Conclusions : Our results suggest a slightly better prognosis, regarding overall survival after RC for patients with NMIBC who progressed to invasive disease, when compared to patients with invasive disease de novo.

Uroflow stoptest following robotic assisted radical prostatectomy can predict intergrity of pelvic floor and return of erectile function

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Introduction et objectifs : To see whether the ability to completely stop urine flow during voiding, measured objectively by uroflowmetry at the time of catheter removal following robotic assisted radical prostatectomy (RARP), can predict integrity of pelvic floor musculature, early recovery of potency and urine continence rates.
Matériels et méthodes : A prospective study was conducted. 108 patients, operated by a single surgeon (AEH), were subjected to a uroflowmetry at the time of catheter removal following RARP. Patients were followed-up for at least 2 years postoperatively. A positive StopTest is defined as the ability to stop urine flow voluntarily for more than 3 seconds provided that a maximum flow of at least 15 ml/sec was reached. Urine continence was defined as 0-pads usage and potency defined as penetration during intercourse.
Résultats : 108 patients were studied. 80 of them were able to stop urine flow (group one) and 28 of them could not (group tow). Age, BMI, IPSS score, tumour stage, prostate volume and estimated blood loss were comparable between the two groups. Nerve preservation status and PSA were statistically higher in group one (p=0.015) and (p=0.042), respectively. The potency rates in group one and group two at 1,3,6,9,12,18 and 24 months were 25% vs. 14.3% (p=0.241), 42.6% vs. 14.8% (p=0.010), 54.5% vs. 18.5% (p=0.001), 56.4% vs. 36% (p=0.084), 66.6% vs. 50% (p=0.141), 65.5% vs. 56% (p=0.404) and 73.2% vs. 57.7% (p=0.160) respectively. Pad-free continence rates in group one and two at 1, 3, 6, 12, 18, and 24 months were 62% vs.7%(p<0.001), 85% vs. 28% (p<0.001), 93% vs. 67% (p=0.001), 93% vs. 82% (p=0.079), 97% vs. 82% (p=0.006), and 97% vs. 85% (p=0.023), respectively. Recovery continence and potency were significantly faster in group one specially in the first 6 months after surgery. The median time to return of urine continence in group one was 1 month , compared to 6 months in group 2 (p<0.001). On the other hand, the median time to intercourse in group one was 4 months, compared to 10.5 months in group tow (p=0.003). Age, BMI and uroflow stop test were statistically significant predictive variables in both univariate & multivariate analysis for early recovery of potency with an OR of 0.869 (IC: 0.776–0.973, p=0.015), 0.741 (IC: 0.583–0.942, p=0.014) and 6.7 (IC: 1.361–32.968, p=0.019), respectively. Nerve preservation was a significant factor in univariate analysis (p=0.046), however, It did not remain as an independent factor in multivariate analysis (p=0.246).
Conclusions : The novel use of Uroflowmetry stoptest at the time of urethral catheter removal is simple, non-invasive and a good indicator of pelvic floor integrity with the ability to predict early recovery of potency and urine continence after RARP. Age and BMI can also predict the recovery of potency.

Estimate the clinical and economic impact of urologists' adherence to the follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma in Canada

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Introduction : Renal cell carcinoma (RCC) represents approximately 3% of all malignancies in Canada. Surgical resection (radical or partial nephrectomy) remains the most effective therapy for clinically localized RCC. However, approximately 40% of patients diagnosed with RCC will develop metastasis and will die of their disease. Surveillance protocols after surgical resection varies depending on the risk of recurrence or development of metastasis.

Objectifs : To estimate the clinical and economic impact of urologists' adherence to the Canadian Urology Association (CUA) guidelines related to the follow-up after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma in Canada as approved in 2009.
Matériels et méthodes : The study cohort was based on the Canadian Kidney Cancer Information System (CKCis). The patients are prospectively recruited since January 2011 in different health centres of seven Canadian provinces. Our cohort includes patients having had radical or partial nephrectomy between January 2011 and January 2014, and a clinical stage of pT1, pT2 and pT3. Kaplan-Meier method was used to evaluate the recurrence rate by urologists' adherence to the CUA follow-up guidelines. Cox proportional hazard model was used to evaluate association between time to recurrence and adherence level adjusted for pathological stage.
Résultats : A cohort of 1,030 patients with an average age of 61 years old (SD ± 12) has been selected. The mean follow-up was 12 months (SD ± 9). During the follow-up, 47.5% of patients have had a number of chest X-ray or CT tests as indicated by the CUA guidelines, whereas 19.8% of patients have had more tests and 32.7% less tests, respectively. The corresponding figures for abdominal CT or ultrasound were 34.7%, 58.9% and 6.5%, respectively. As per CUA guidelines the total number of chest X-ray or CT and abdominal CT or ultrasound in this cohort should have been 960 and 332, respectively. The actual imaging test counts were 754 and 1,478, respectively. Two-year recurrence rate was 27% in patients with more abdominal CT or ultrasound than recommended by guidelines, and 20% in the others ($p<0.0001$). When adjusted for pathological stage, a hazard ratio of 3.1 (95%CI: 2.1–4.6) was estimated for patients with more abdominal CT or ultrasound than recommended by guidelines compared to the others.
Conclusions : Our study shows important differences in type and number of imaging tests between CUA guidelines and actual clinical practice. The results suggest that clinicians have performed a more intense surveillance in patients with poor clinical outcomes. Further analysis should be performed after a longer duration of follow-up to evaluate survival in these patients.

Permanent seed brachytherapy or external beam radiation for clinically localized prostate cancer: Results of 1000 patients from a single institution

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Introduction et objectifs : To analyze biochemical outcome in patients with D'Amico low, intermediate and high-risk prostate cancer treated with different radiation techniques.
Matériels et méthodes : We analyzed 1000 patients treated at our institution with a minimum follow-up of 36 months from 2001–2012 out of which 50% were treated prior to 01/2008. 58% of patients were treated with external beam radiotherapy (EBRT) and 42% with permanent seed prostate brachytherapy (BT) either as monotherapy or in combination with EBRT. In total, 40% of patients were treated in phase II-III trials for EBRT. Dose levels varied from extreme hypofractionation (45 Gy in 9 weekly fractions) to 79.2 Gy (in 1.8–2.0 Gy per fraction). Cox regression analysis was used for investigating the influence of the D'Amico classifications and the CAPRA score to predict for biochemical failure (bF), as per the Phoenix definition (PSA-nadir + 2 ng/mL).
Résultats : Mean age was 67.3 years (SD 6.5). D'Amico low, intermediate and high-risk cancers were present in 460 (46%), 466 (47%) and 74 (7%) of patients. One hundred and eleven patients (11%) experienced bF at a mean of 48 (SD 25) months following treatment. Median follow-up for patients without bF was 60 months. The 5- and 7- year biochemical recurrence free survival for low risk cancers were respectively, 95% and 91%, for intermediate risk 89% and 78% and for high-risk cancer 92% and 72% ($p=0.002$, log-rank test). In a multivariate cox regression analysis adjusted for treatment type (BT vs. EBRT), PSA as a continuous variable (HR 1.03, 95%CI 1.01–1.05, $p=0.001$) and Gleason score (HR 1.42, 95% CI 1.09–1.85, $p=0.01$) were both predictive of bF, but not T-stage or age. The CAPRA score grouped into scores of 0–2, 3–5 and 6–10 was predictive of bF adjusted for treatment type ($p<0.001$). We conducted a multivariate cox-regression analysis in patients with intermediate risk cancer, comparing dose levels of EBRT of ≥76 Gy (n=193), 70–74 Gy (n=82), hypofractionation with 57–60 Gy in 3 Gy per day (n=123) and BT (n=123). BT was superior to all EBRT dose-levels (HR for EBRT 5.4–10.4, $p=0.003$–0.022). Antiandrogen therapy (in 13% of patients) was also significant (HR 0.45, 95% CI 0.21–0.998), $p=0.049$) as well as the CAPRA score as a continuous variable (HR 1.55, 95%CI 1.27–1.90, $p<0.001$).
Conclusions : Results from our large database show high biochemical cure rates for all risk stages after a median follow-up of 5 years. Although there was no central pathology review, Gleason score and PSA are the most important individual prognostic factors.