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1. Simultaneous Determination of Morphine, Morphine Glucuronides (M3G, M6G) and Oxycodone in Human Plasma by High-performance Liquid Chromatography

Morphine and oxycodone are widely used as analgesic drugs for cancer pain. Frequently, morphine and oxycodone are given alternately to avoid adverse drug reactions. Morphine is metabolized primarily into two glucuronide metabolites, morphine-3-glucuronide and morphine-6-glucuronide to be pharmacologically active. Morphine-3-glucuronide and morphine-6-glucuronide have neuroexcitatory action and analgesic activity, respectively. Oxymorphone, a metabolite of oxycodone, has an analgesic effect, however it is so small that it can be neglected when considering oxycodone. The pharmacological effects of these drugs and also their metabolites have been reported in experimental papers, but in humans, the relationships between these plasma concentrations and the clinical effects remain unclear. Also the necessity for simultaneous determination of both drugs has been suggested because opioid rotation is performed clinically. However, to date there is no study which has simultaneously determined these four drugs, and also achieved a high recovery. In this paper, in order to perform a reliable pharmacokinetic study of cancer pain patients receiving morphine and oxycodone, an easy, rapid, sensitive and selective analytical method was proposed and validated.

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2. Development and Validation of a Liquid Chromatography Method for the Analysis of Paromomycin Sulfate and its Impurities

A rapid and simple method for the separation and quantification of paromomycin sulfate and its impurities by HPLC coupled with evaporative light scattering detection (ELSD) was developed. The chromatographic conditions included the use of a GRACE Alltima C18 column (250 mm×4.6 mm, 5 µm) maintained at 30°C and a mobile phase of 0.2 M trifluoroacetic acid water–acetonitrile (96:4, v/v) at a flow rate of 0.6 mL/min. The influence of gas pressure and temperature of the drift tube in the detector on the detection response was also investigated. A system suitability test to check the quality of the separation was specified. The method showed good repeatability, linearity and robustness. It also enabled the simultaneous determination of the inorganic counter ions (sulfates).

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3. Effect of Temperature, Wavelength, pH, Ion Pair Reagents and Organic Modifiers' Concentration on the Elution of Cystatin C. Stability of Mobile Phase

Robustness of an analytical chromatographic method for separation of cystatin c has been verified. Changes in many parameters were carried out, such as, wavelength, column oven, mobile phase composition, chromatographic column.

Imperative changes have altered the efficiency of the chromatographic separation; such changes include pH alteration of the mobile phase as well as alkyl sulfonate molarity changing.

All robustness conditions showed no major effect on the chromatographic separation of the analyte except with the changes related to TFA and alkyl sulfonate ion pair reagents. Peak area RSD, asymmetry and No. of theoretical plates were <0.7%, <1.2 and >10,000, respectively. Results obtained using mobile phase after 6 months of storage have proven its stability and possibility of use. Gradient elution mode was utilized to elute cystatin c with a UV detection of 224 nm. Ace and Waters C8 (150×4.6 mm i.d., 5 µm) as chromatographic columns were used.

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4. Development and Validation of a Liquid Chromatographic/Mass Spectrometric Method for the Determination of Saikosaponina in Rat Plasma and its Application to Pharmacokinetic Study

A rapid and sensitive liquid chromatography/mass spectrometry (LC/MS) method was developed and validated for the determination of saikosaponina in rat plasma. Saikosaponina was extracted by protein precipitation with acetonitrile and the chromatographic separation was performed on a C18 column. The total analytical run time was relatively short (5.5 min) and the limit of assay quantification (LLOQ) was 10 ng mL^{-1} using 100 µL of rat plasma. Saikosaponina and the internal standard (felodipine) were monitored in selected ion monitoring (SIM) mode at m/z 779.2 and 382.0, respectively. The standard curve was linear over a concentration range from 10 to 5000 ng mL^{-1} and the correlation coefficients were greater than 0.999. The recoveries of saikosaponina from plasma were larger than 82% and RSD of inter-day and intra-day assay were below 10%. The method described in this report was sensitive and specific and suitable for pharmacokinetic studies of saikosaponina in rats.

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5. Determination of Glipizide, Glibenlamide and Glimeperide in a Tablet Dosage Form in the Presence of Metformin Hydrochloride by Ion Pair –Reversed Phase Liquid Chromatographic Technique

The present work describes the development and validation of an isocratic HPLC method for the stability indicating assay of Glipizide (GPZ), Glibenclamide (GBD) and Glimeperide (GMD) in the presence of Metformin hydrochloride (MET) in pharmaceutical dosage forms using ion pair-reversed phase liquid chromatographic Technique. The ion pairing agent used was tetrabutyl ammonium hydrogen sulphate (TBHS). The TBHS 0.030 molar solution in water with pH 6.0 used as buffer. The composition of buffer with acetonitrile used was 50:50 (v/v) on reversed phase column bonded with octadecylsilane. The wave length used was 225 nm. The resolution between the closest peaks Glimeperide and Glibenclamide was more than 1.5 and all the three drugs gives a linear response (r^2>0.999). The method used for all the three substances were found selective, precise, accurate and robust. The method can be used for quality control assay of the bulk and in finished dosage form as single component and combine with Metformin hydrochloride. The purpose of the method to study individually the stability of Glipizide, Glibenclamide and Glimeperide in the presence of Metformin hydrochloride as any such method is not reported so far.

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6. Ionization Polarity as a Cause of Matrix Effects, its Removal and Estimation in ESI-LC-MS/MS Bio-analysis

Matrix effect is the effect on an analytical method caused by all other components of the sample except the specific compound to be quantified. Matrix effects and selectivity issues have long been associated with bioanalytical techniques. A number of approaches have been investigated to improve reproducibility and robustness of LC-MS-MS methods that are subjected to matrix effects. In the present research work the role of ionization polarity on matrix effect was studied. Enalapril and its metabolite were analyzed in positive and negative polarity by using ESI-LC-MS/MS. Matrix factor (MF) was determined to evaluate the matrix effects in different polarities. Two different concentration levels of each analyte were used to determine the MF. In positive polarity the MF at two different concentration levels were 0.6353 & 0.6496 for enalapril and 0.6885 & 0.6770 for enalaprilat, whereas, the MF in negative polarity at two different concentration levels were 0.8203 & 0.7717 for enalapril and 1.1124 & 1.0915 for enalaprilat. These data showed approximately 30-35% ion suppression in positive polarity for both the analyte, but approximately 20% ion suppression for enalapril and 10% ion enhancement for enalaprilat in negative polarity. So, matrix effects depend on the ionization polarity also.

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7. GC/MS Determination of N-butyl-N-(3-carboxypropyl) Nitrosamine (BCPN) in Bladder Cancers-The Skewed Molecular Interaction Caused Retention Time Shift

N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN) has been widely used in rodents as an invaluable experimental tool for investigation of bladder cancer (BCA). The urinary level of its metabolite, N-butyl-N-(3-carboxypropyl) nitrosamine (BCPN) was reported to be a very reliable predicative parameter of BCA. However, in determination of the urinary BCPN we found the retention time (t_R) of BCPN was randomly damping. The t_R values of the authentic BCPN at 5, 10, 20, 50, and 100 ppm were 28.48, 27.59, 27.43, 28.00, and 28.32 min comparing with 28.23 min of the urinary BCPN in HPLC analysis, similarly, 17.30 min for the urinary and the 18.00 min for the authentic BCPN in GC/MS analysis. To interpret such a damping, we theoretically proposed that a certain transient skewed molecular interaction could occur during the chromatographic separation, which would cause a certain degree of fluctuation on the t_R of target molecules. Conclusively, the retention time of a chemical is not a definite value as often considered in HPLC and GC/MS analyses. In reality it fluctuates depending mainly upon the interaction among a cluster of coexisting molecules, in particular, when operated at higher concentrations.

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8. Development and Validation of a Stability-Indicating HPLC Method for the Simultaneous Determination of Salbutamol Sulphate and Theophylline in Pharmaceutical Dosage Forms

The study describes development and subsequent validation of a stability indicating reverse-phase highperformance liquid chromatography method for the simultaneous estimation of salbutamol sulphate and theophylline in tablet dosage forms. A reversed-phase phenomenax C-18 column (250 mm×8 mm i.d., particle size 10 µm) column with mobile phase consisting of acetonitrile and phosphate buffer 65:35 (v/v) (pH 4.2 ± 0.02, adjusted with triethylamine) was used. The flow rate was 1.2 mL min^{-1} and effluents were monitored at 235 nm. The retention times (t_R) of salbutamol sulphate and theophylline were found to be 5.33 min and 13.36 min, respectively. The method was validated in terms of linearity, range, specificity, accuracy, precision, limit of detection (LOD) and limit of quantitation (LOQ). The linearity for both the drugs was found in the range of 2-64 µg mL^{-1}. The % recoveries of salbutamol sulphate and theophylline were found to be 99.41 and 101.11, respectively. The utility of the procedure is verified by its application to marketed formulations that were subjected to accelerated degradation studies. The method distinctly separated the drug and degradation products even in actual samples. The products formed in marketed tablet dosage forms are similar to those formed during stress studies.

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9. Development and Validation of Spectrophotometric and HPLC Method for the Simultaneous Estimation of Salbutamol Sulphate and Prednisolone in Tablet Dosage Form

Simple, accurate, and reproducible UV spectrophotometric and HPLC method for simultaneous estimation of salbutamol (SAL) and prednisolone (PRE) was developed in the present work. The first developed method was Simultaneous equation method, wavelength selected are 227 nm for salbutamol and 244 nm for prednisolone respectively. Linearity was observed in concentration range of 6-20 µg/ml for salbutamol as well as for prednisolone. Second developed method was RP-HPLC method using Thermo C18 column (4.6 mm i.d×250 mm) and acetonitrile: 0.025M potassium dihydrogen orthophosphate buffer (pH adjusted to 3.5 with orthophosphoric acid) in the ratio of 30:70% v/v as mobile phase. For HPLC method, linearity was observed in the concentration range of 20-100 µg/ml for salbutamol as well as for prednisolone and drugs was subjected to oxidation, hydrolysis, and heat to apply stress condition for degradation studies. Results of analysis were validated stastically and by recovery studies.

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10. Determination of Tacrolimus in Rat Whole Blood Utilizing Triple Quadrupole LC/MS

A simple, sensitive and rapid method was developed for quantitation of tacrolimus in rat whole blood utilizing triple Quadrupole LC/MS. An aliquot of 0.1 mL of whole blood sample was extracted with t-butyl methyl ether using a Heidolphvortexer. The chromatographic separation was performed by using chromolith fast gradient HPLC RP 18e (2 mm×50 mm.i.d) column with a mobile phase of 90% methanol and 10% 2 mM ammonium acetate buffer followed by MS/MS detection. The analyte was quantitated in negative ionization mode. Multiple reaction monitoring (MRM) using the transition m/z 802.4→560.2 and m/z 808.4→548.6 was performed to quantify tacrolimus with IS (pimecrolimus), respectively. The method had a total chromatographic run time of 2.5 min; and linear calibration curves over the concentration range of 20.931-1000.703 ng/mL.The lower limit of quantification (LLOQ) was 20.931 ng/mL. Use of sodium citrate (3.85%) as an anticoagulant in rat whole blood and samples were stable for at least the time required to assay the number of samples that could be placed in the auto sampler which is maintaining temperature of 10°C. The between and within batch precision and accuracy of the method were determined by using 6 quality control samples. The highest % CV 478.908 ng/mL (8.01% within run & 3.07 between run), with other % CV<5%. The recovery ranged 23.92% for tacrolimus over range of 50.285 to 798.179 ng/mL and was 18.52% for pimecrolimus respectively. The validated method was successfully applied to the quantification of tacrolimus concentration in rat whole blood.

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11. HPTLC Method Validation for simultaneous determination of Tamsulosin Hydrochloride and Finasteride in Bulk and Pharmaceutical Dosage Form

A new simple, precise, accurate and selective TLC-densitometry method has been developed for simultaneous determination of tamsulosin hydrochloride and finasteride in tablet dosage form. Chromatographic separation was performed on aluminum plate precoated with silica gel 60 F254 using toluene: n-propanol: triethylamine (3.0:1.5:0.2 v/v) as mobile phase. Detection was carried out densitometrically at 260 nm. The RF value of tamsulosin hydrochloride and finasteride were 0.32 and 0.54, respectively. The reliability of the method was assessed by evaluation of linearity which was found to be 200-1200 ng/spot for tamsulosin hydrochloride and 1000-6000 ng/spot for finasteride. Accuracy of the method was accessed by percentage recovery and found to be 99.77 ± 0.71 % for tamsulosin hydrochloride and 99.75 ± 0.86 % for finasteride. The method can be used for routine analysis of tamsulosin hydrochloride and finasteride in tablet dosage form.

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12. Estimation of Pharmacokinetics of Propofol in Indian Pateints by HPLC Method

A quick and sensitive reversed phase high performance liquid chromatography (HPLC) method has been developed in Indian surgical patients to determine the concentration of Propofol In human plasma. Propofol can be isolated from human plasma by adding 1 ml precipitating solution which consists of acetonitrile and perchloric acid (67:33) mixture, which also contains dibutylpthalate (1 mg/ml) as an internal standard. The sample is mixed for two minute on a vortexer. The plasma substance precipitated by acetonitrile and perchloric acid are further separated by centrifugation. The supernatant is directly injected into the HPLC system with the help of autosampler.

The analysis was carried out using column 250×4.6 mm column packed with10-µm Spherisorb reversed phase octadecylsilane particles (C18). The 500 ml of mobile phase (67:33:0.04) consisted of 335 ml of acetonitrile and 165 ml of distilled water and 200 µl of acetic acid maintaining the pH 4.0.The flow rate of the mobile phase was 1.5 ml/min. propofol was monitored by a UV detector at a 270 nm wavelength. The limit of detection of propofol (in human plasma) was found to be 0.0001 µg/ml while limit of quantification was found to be 0.001 µg/ml for a 20 µl injection volume.

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13. Difference in Absolute CD4+ Count According to CD4 Percentage between Asian and Caucasian HIV-Infected Patients

We compared the absolute CD4+ count, at different CD4+ percentages (CD4%), between Asian (n=442) and Caucasian (n=674) untreated HIV-infected individuals, using linear regression methods. At any given CD4%, Asians had lower CD4+ count than Caucasians (p=0.001). The difference varied from 38.9 cells/mm^3 (95% CI: 3.3-74.5 cells/ mm^3) at CD4% of 15% to 108.7 cells/mm^3 (95% CI: 42.5-174.9 cells/mm^3) at CD4% of 40%. The impact of these differences on prognosis is uncertain, but it may be that the prognostic thresholds for CD4+ count used in Caucasian populations are inappropriate in Asian populations.

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14. Characteristics of Natural Killer Cells in Malaysian HIV Patients Presenting with Immune Restoration Disease after ART

Objectives: Natural killer (NK) cell function was investigated in Malaysian HIV patients beginning antiretroviral therapy (ART) with advanced immunodeficiency. Some patients experienced immune restoration disease (IRD) presenting as exacerbations of pre-existing infections. Whilst most IRD are attributed to interferon-gamma (IFNγ) produced by T-cells, NK cells may also contribute.

Methods: Blood leukocytes were collected prospectively from 100 HIV patients over 1 year on ART, plus 36 healthy controls. Eleven patients who experienced an IRD and 14 matched controls were assayed. Cells producing IFNγ were quantitated by ELISpot after stimulation with an NK target (K562 cells) or antigens from pathogens associated with the IRD. NK cell subsets, CD16 and perforin expression were determined by flow cytometry

Results: NK cell IFNγ responses were lower in HIV patients at baseline ($p<0.001$), improved by Week 24 ($p<0.01$) but remained lower than uninfected controls ($p<0.05$). Proportions of CD56hi NK cells increased ($p<0.01$) above controls at Week 24. Perforin expression on these cells was higher than controls at baseline ($p<0.01$), but declined on ART. Proportions of CD56hl NK cells were similar in patients and controls throughout. IRD patients showed lower CD16 expression on CD56lo NK cells than non-IRD patients before treatment ($p<0.05$)

Conclusions: NK cells profiles were restored on ART, but NK cell IFNγ production remained impaired. Low CD16 expression on CD56lo NK cells may mark a predisposition for an IRD.

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15. Simplification with Fixed-Dose Tenofovir-Emtricitabine or Abacavir-Lamivudine in Treatment Experienced, Virologically Suppressed Adults with Hiv Infection: Combined Analysis of Two Randomised, Non-Inferiority Trials Bicombo and Steal

Background: There is uncertainty about the comparative safety and efficacy of the fixed-dose-combination tablets tenofovir 300mg+emtricitabine 200mg (TDF/FTC); and abacavir 600 mg+lamivudine 300 mg (ABC/3TC).

Methods: We used random effects meta-analysis to compare 96 week data for ABC/3TC and TDF/FTC randomised arms from the BICOMBO (n=333) and STEAL (n=357) treatment experienced and virologically suppressed switch studies. Endpoints included: virological failure (VF, repeat plasma HIV RNA>400 copies/mL); mean change to week 96 in CD4 and metabolic parameters; proportion with serious non-AIDS events (SNAEs, retrospectively collected in BICOMBO). We used exact statistics for relative difference in proportions (RD), and ANOVA for differences between means. Difference was for ABC/3TC minus TDF/FTC.

Results: There was no significant difference between arms in VF (RD% 0.7 95%CI-3.4, 4.8). Change from baseline in CD4 was of marginal significance (ITT 0.16 cells/mL 95%CI 0.0, 0.32). Mean change in HDL, LDL, total cholesterol triglycerides were significantly greater in the ABC/3TC arm ($p<0.01$ for all), there was no difference in total cholesterol:HDL ratio (0.11 95%CI-0.16, 0.29). There was a greater proportion of SNAEs in the ABC/3TC arm (relative difference 3.8%, 95%CI 0.1, 7.6) primarily arising from the STEAL study.

Conclusions: In a switch study setting ABC/3TC based therapy was virologically non-inferior over 96 weeks to TDF/FTC based therapy. Lipid markers were generally elevated in the ABC/3TC arm.

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16. Holmes´ Tremor in an HIV Positive Patient Worsened by Immune Recovery Inflammatory Syndrome (IRIS)

IRIS is characterized by a paradoxical deterioration of clinical status after initiation of Anti-Retroviral Therapy (ART), despite improved immune function. It is caused by inflammatory response against the infectious antigen. IRIS typically occurs in patients with a low initial CD4 (usually <50) and a rapid decline in viral load. It is seen within a broad spectrum of HIV-related opportunistic infectious diseases and autoimmune disorders in patients who had been given Highly Active Anti-Retroviral Therapy (HAART). Our objective is to describe an HIV positive patient with Holmes´ tremor worsened by IRIS, with marked recovery after therapy with steroids.

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17. Seronegative HIV-1 Infection, a Difficult Clinical Entity; a Case Report

Patients infected with HIV typically seroconvert within weeks of primary HIV infection. In rare cases, patient do not develops antibodies despite demonstrable HIV infection by p24 antigen or viral load assays; a seronegative HIV. Very few such cases been reported so far in the literature. Seronegative HIV is many times difficult to differentiate from acute seroconversion illness due to HIV in clinical practice. Here we are describing such case with clinical dilemma.

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18. Barriers to ARV Adherence among HIV/AIDS Positive Persons taking Anti-Retroviral Therapy in Two Tanzanian Regions 8-12 Months after Program Initiation

The purpose of this study was to measure adherence and to identify specific factors facilitating or constraining adherence to anti-retrovirals (ARVs) among HIV/AIDS patients. A cross sectional study on ARV adherence was conducted in two Tanzanian regions, Arusha and Dar es Salaam, in June and July 2005, involving 7 healthcare facilities in these regions. A multi-disciplinary team of researchers collected the data from two populations: the ARV users and the health care providers. The data was collected from the ARV users through exit interviews, semi structured interviews, adherence measures, focus group discussion and key informants interviews. From the health care staff, the tools used were semi structured interviews, observation of staff conducting consultations, and pharmacy stock check-ups. A total of 207 ARV users were studied, 26 observations were made, 28 health staff were interviewed, 8 focus group discussions and 10 key informant interviews were conducted, and 6 pharmacy stock checks were done in healthcare facilities.

Results from the qualitative discussions, individual as well as institutional factors contributed to non-adherence. For many food, long waiting time, transportation, social supports, lack of education about anti-retroviral therapy (ART) or ARVs, lack or inadequate counseling, drug related side effects, and even knowledge about AIDS were barriers. Structural impediments such as stigma by untrained hospital care workers towards clients, over worked health care staff, and lack of space for confidential consultations, lack of availability of diagnostic and laboratory equipments were also sited as barriers. However, according to health staff, adherence was interpreted to mean using medicines as prescribed, at the right time and at the correct dosage, and attending the facilities as scheduled for follow-up checks.

Many patients are appreciative of the government and of the health care workers involved in the programs. Yet, close attention and adequate supplies and resources to overcome the external barriers and attempts to try to mitigate the internal negative social determinants which prohibit adherence are needed. Unless due attention is paid to the critical issue of adherence, the emergence of drug-resistance will be accelerated and the expected early treatment achievements could be reversed.

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19. A Prospective, Double Blind, Randomised, Placebo Controlled Trial Evaluating Acetyl-L-Carnitine (ALCAR) for the Prevention of Distal Symmetric Polyneuropathy in HIV Infected Individuals

Background: Nucleoside reverse transcriptase inhibitors (NRTIs) are currently an essential part of highly active antiretroviral therapy (HAART) for the treatment of HIV. However, the use of some dideoxynucleotide analogues may be limited by mitochondrial toxicity leading to distal symmetric polyneuropathy (DSP). Acetyl-L-Carnitine (ALCAR) has been investigated for the treatment of existing DSP but the potential for ALCAR to prevent DSP is unknown.

Methods: In this double blind, placebo controlled trial 43 HIV infected, antiretroviral naïve individuals were randomised to receive either ALCAR or placebo in addition to stavudine (as stavudine-XR, a sustained release formulation), tenofovir and efavirenz for 48 weeks. Development of DSP was assessed clinically and histologically by Protein Gene Product (PGP) staining of the epidermis. Quality of life (QOL) was measured during the study with the MOS-HIV Health Survey and the QUROQOL Score questionnaires.

Results: Twenty one subjects in each treatment arm were followed through 48 weeks. Discontinuation rates for stavudine and ALCAR versus placebo were similar in both groups. No differences were found for histological examination or clinical assessment of DSP; whilst the safety profile of ALCAR was comparable to placebo.

Conclusions: At 48 weeks the prophylactic administration of ALCAR with HAART to prevent DSP was no different than placebo, with a similar safety profile.

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20. Two-Year Observational Study in Patients Infected with Drug-Resistant HIV-1 and Treated with the Fusion Inhibitor Enfuvirtide: The ZOOM Cohort

The objective of this study was to describe, in real-life settings, the patients treated by the HIV fusion inhibitor enfuvirtide and to evaluate efficacy and safety of this new antiretroviral drug in comparison with the results of the pivotal studies TORO 1 and TORO 2.

Adult HIV-1-infected patients, treated for the first time with enfuvirtide since less than 2 months, were eligible for the study. From September 2004 to May 2006, 364 patients (male, 81%) with a mean (SD) age of 45 (9) years and at CDC stage C for 52% of them were included and followed for 2 years. The median duration of antiretroviral treatment was 10 years with a median number of 11 drugs. Median HIV viral load was 4.7 log10 copies/mL and median CD4 cell count was 155 cells/mm^3 (respectively, 5.2 log10 copies/mL and 89 cells/mm^3 in TORO studies). Compared to the TORO studies, the proportion of patients on enfuvirtide treatment with HIV RNA <400 copies/mL in ZOOM study was higher (61 vs. 34% at 1 year; 77 vs. 48% at 2 years). The immunologic benefit was approximately the same at 2 years (+173 cells/mm3 in ZOOM vs. +166 cells/mm^3 in TORO studies). Bacterial pneumonia was reported for 5 patients (0.81 case for 100 patient-years).

In conclusion, in real-life settings, the results of the ZOOM study at 2 years confirmed the virologic and immunologic benefits and the favorable safety of enfuvirtide reported in the TORO pivotal trials.

Pancytopenia with Hemophagocytic Syndrome Associated with Histoplasmosis in Acquired Immunodeficiency Syndrome: Description of 2 Case Studies and Literature Review

Two cases of haemophagocytic syndrome (HPS) due to histoplasmosis in patients with the acquired immunodeficiency syndrome (AIDS) are described in our case studies. Both the patients presented with pancytopenia and the bone marrow aspirate showed features suggestive of haemophagocytosis and the presence of intracellular inclusions were compatible with Histoplasmacapsulatum. Haemophagocytic syndrome due to disseminated histoplasmosis should be included in the differential diagnosis of pancytopenia in patients with AIDS, though it is a rare clinical entity.

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21. Drug Resistance Patterns and Virus Re-Suppression among HIV-1 Subtype C Infected Patients Receiving Non-Nucleoside Reverse Transcriptase Inhibitors in South Africa

Background: Emergence of HIV-1 drug resistance is at times an inevitable and anticipated consequence of antiretroviral therapy (ART) failure. We examined drug resistance patterns and virus re-suppression among subtype C-infected South African patients receiving first-line ART.

Methods: Treatment records of 431 patients on NNRTI-containing regimens for a median of 45 months were analyzed. Patients with viral load (VL) >400 copies/mL were followed and drug resistance mutations (DRM) were re-assessed. Associations between clinical/demographic measures and drug resistance/virologic outcomes were examined using Fisher exact and ordinal and logistic regression.

Results: Ten percent of patients (43/431) were viremic at enrollment (98%) sequences were obtained from 38/43. Of those, 82% had 1-7 DRM. In bivariate analysis remote exposure to single-dose nevirapine or prior ART; higher CD4 counts; lower VL; and >6 months of virologic failure were significantly associated with number of DRM. Of 25 viremic patients followed for a median of 8 months on a continued first-line regimen, 12 (48%) re-suppressed, six with K103N and three with M184V. Thirteen (52%) had continued virologic failure which was significantly associated with detectable VL >6 months prior to enrollment and number of DRM.

Conclusion: Among these HIV-1 subtype C-infected patients, DRM numbers and patterns were associated with prior exposure to sub-optimal ART, adherence and duration of virologic failure. Viral re-suppression in the presence of K103N and M184V challenges assumptions about drug resistance. In resource-limited settings, where genotyping and alternative drug options are unavailable, continuing first-line treatment, reinforcing adherence and regular virologic monitoring may be effective even after virologic failure.

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22. Hot Immunological Topics in HIV Infection

Incomplete immune reconstitution and persistent immune system hyperactivation in spite of highly active antiretroviral therapy continue to be a challenge. Both facts may lead to an increased risk for AIDS-defining and non AIDS-defining clinical conditions and may also promote atherogenesis and liver fibrogenesis in HIV and hepatitis C virus-coinfected patients. In this article, the use of new markers to assess immune reconstitution and immune activation and the incidence and clinical consequences of immunediscordant response to antiretroviral therapy are addressed. Likewise, the impact of immune dysfunction on atherogenesis and liver fibrogenesis are reviewed. Finally, it is discussed whether therapy with drugs belonging to the family of CCR5 inhibitors may provide additional immunological benefit in HIV-infected patients.

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23. Primary Human Immunodeficiency Virus Infection and Rhabdomyolysis

Objectives: Over the past few years we have seen 3 patients with primary HIV infection and rhabdomyolysis in our institution.

Methods: We report our 3 cases in addition to the review of the English-language literature for all reported cases of rhabdomyolysis and primary HIV infection.

Results: In addition to our 3 cases we found 11 cases of primary HIV infection presenting with rhabdomyolysis.

Conclusion: In patients presenting with rhabdomyolysis and no obvious precipitating factor, primary HIV infection should be included on the differential count.

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24. Factors Associated with Recent Risky Drug Use and Sexual Behaviors among Drug Users in Southwestern China

A cross-sectional survey was conducted in 2007 among 504 drug users who were recruited mainly from detoxification centers in southwest China. About one-third (34.3%) of participants reported recent risky drug use behavior, which was defined as injecting drugs in the past 3 months, and more than one-fifth (21.6%) reported recent risky sexual behavior, or had multiple sexual partners in the past 30 days. Male sex (odds ratio [OR], 1.9; 95% confidence interval [CI], 1.2-3.2) and more episodes of detoxification (OR, 3.7; 95% CI, 2.3-6.0) were associated with higher odds of risky drug use behavior, while unmarried status (OR, 1.7; 95% CI, 1.0-2.9), higher personal annual income (OR, 1.8; 95% CI, 1.1-2.8) and history of sexually transmitted infections (OR, 3.7; 95% CI, 2.1-6.6) were associated with higher odds of having risky sexual behavior. Subgroup analyses showed 15% participants who used drugs in the past 3 months also shared needles, and 77% participants who had multiple sexual partners in the past 30 days did not use condoms during sex with non-primary sexual partners. The study findings are useful for developing HIV risk reduction intervention programs among drug users.

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25. Amphotericin B as Alternative to Itraconazole in Secondary Prophylaxis of Neurohistoplasmosis in HIV-Positive Patients with Antiretroviral Therapy

Histoplasma is a dimorphic pathogenic fungus wich causes human infection worldwide, mainly in ecuatorial countries. In immunocompetent patients the most commun clinical manifestations consist in a lack of symptoms or a self-limited flu-like profile. However, disseminated histoplasmosis, wich represents the 0.05% of the acute infections, is observed in immunosuppressed patients (most of them HIV infected or treated with immunosuppressive drugs), and the illness manifestations are indistinguishable from tuberculosis. Central nervous system (CNS) involvement is exceptional and affects 5-10% of patients with disseminated illness and only 26 previous cases of meningitis caused by this microorganism were described in the last decade. The majority of these patients are treated with nonnucleoside reverse-transcriptase inhibitors, and it is necessary to notice that interaction between this drugs and itraconazole (used in the prophylaxis of these infections) exists. Although this drug-drug interaction is really presumed, the international literature review using MEDLINE database and EMBASE (keywords: interaction ± itraconazole ± nonnucleoside ± reverse-transcriptase ± inhibitors) showed only 3 previous cases. It is interesting to report here, because of its rareness, one case of acute meningitis due to *Histoplasma*, whose treatment and prophylaxis failed initially because of drug-drug interaction between itraconazole and nonnucleoside reverse-transcriptase inhibitors.

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26. Intestinal Histoplasmosis with *Histoplasmaduboisii* in a Patient Infected by HIV-1 in Abidjan (Ivory Coast)

We report a case of intestinal histoplasmosis with *Histoplasmaduboisii* in a 39-year-old patient infected with HIV-1, admitted to the emergency department due to peritonitis with fever and weight loss. He underwent a right hemicolectomy, and the pre-perforation and ulcerated macroscopic aspect during surgery suggested a malignant tumor. The anatomopathological examination of the specimen removed revealed the presence of inflammatory granulomas containing *Histoplasmaduboisii* yeasts. The evolution was rapidly unfavorable, culminating in the patient's death 12 days after treatment onset with intravenous amphotericin B associated with an antiseptic biantibiotherapy. The authors point out the rarity of intestinal localization of histoplasmosis in patients infected with HIV in Abidjan and the contribution of anatomopathological examination in the diagnosis of this condition.

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27. Physical Activity Measurements Using Accelerometers and Pedometers in HIV-Infected People

Research suggest that physical activity (PA) is inversely related to numerous metabolic disorders in people who are living with HIV. Objective and accurate measurement of habitual PA in this population is essential for a better knowledge of the relationship between PA levels and health benefits. Pedometers and accelerometers are widely use in exercise science to obtain objective measurements of PA. This systematic review has been focused on the use of pedometers and accelerometers in HIV-infected population in order to verify the PA levels. The actual recommendation for healthy people of ≥ 10,000 steps•day-1 is unrealistically high for the population living with HIV. Compared with previous reports on healthy adults, people living with HIV have lower levels of PA. Few studies have assessed PA level using pedometers and accelerometers in people who are living with HIV, so it is not possible define the real PA patterns of HIV-infected yet because there is a lack of information about this issue. Future studies should assess PA objectively (pedometers and/or accelerometers) in people who are living with HIV in order to improve knowledge of PA levels and its relationship with health benefits.

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28. Prevalence of Paediatric HIV Infection in Eastern India-First report

Prevalence of pediatric HIV has not been well characterized. We evaluate the prevalence, risks and contributing factors to the spread of HIV in India. This manuscript aims to describe prevalence of Pediatric HIV infection in Eastern India. We want to provide data on burden of HIV positive children visiting a tertiary care center located in the city of Kolkata, East India. Data is provided for routes of HIV exposure and occupational background and HIV status of the parents of infected children.

Background: Various studies in India have documented high prevalence of HIV infection in children. Nearly 20 million babies are born each year and the number of infected babies could be >50,000 per year. According to Solomon S et al in India the prevalence of HIV among pregnant women varies widely from state to state and figures range from 0.5% to as high as 4.7% as in Namakkal, a small village in Tamilnadu.

Objective: To determine and characterize the prevalence of pediatric HIV/AIDS in India

Methods: This is a two year retrospective review of patients from the (with 100 beds) pediatric outpatient unit of the Medical college and Hospital, Kokata, was undertaken to determine the prevalence of pediatric HIV/AIDS in East Kolkata (or in North India).

Results: 3,669 pediatric patients were admitted to the hospital, 437(11.9%) tested positive for HIV, 234 were males, while 203 were females (m:f=1.15:1). Children under the age of five years accounted for 81.7% of the HIV positive children. Mother-to-child transmission occurred in 73.7% of cases was the major route of transmission of HIV. Two other common routes included the use of blood/blood products (21 patients), hairdressing implements due to punctures in 4.8% each, while sexual abuse/sex activities were the probable route in 3.8% others. Most mothers of HIV children were either housewives (45.3%), or petty traders, trade that is conducted on a small scale (10.4%).

Conclusion: The prevalence of pediatric HIV/AIDS was high in Eastern india. The most common mode of transmission was mother to child. Programs to work on education of prevention of this mode of transmission should be implemented by proper detection of disease in mothers,adequatecounselling and administration of HAART to prevent mother to child transmission of AIDS.

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29. Contraceptive Counseling and Use among Women with Poorer Health

Background: To explore associations between health status, contraceptive counseling and contraceptive use.

Methods: Women aged 18-50 visiting one of 4 primary care clinics were invited to complete surveys after their visit. Perceived health status was measured using a 5-point scale. Among those considered at risk of unintended pregnancy, logistic regression was used to investigate associations between health status and contraceptive counseling and use.

Findings: Women reporting poorer health had decreased odds of receiving some contraceptive counseling at their visit (aOR=0.62, CI=0.39, 0.97) and using some contraception at last intercourse (aOR=0.63, CI=0.41, 0.97) compared to women reporting better health. However, among women with poorer health, receipt of counseling about hormonal contraception was associated with increased odds of using hormonal methods (aOR=8.22, CI=1.77, 38.19). Only 7% of women in poorer health received counseling on highly effective reversible contraception.

Conclusions: Women in poorer health may be at risk of adverse reproductive health outcomes and should receive counseling on safe hormonal and highly effective reversible contraceptives.

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30. Phrygian Cap Appearance of a Mouse Gallbladder on Magnetic Resonance Imaging

We used live-animal magnetic resonance imaging (MRI) to examine the gallbladders of male mice. These healthy mice were fasted overnight before the study and anesthetized in an animal chamber, with a gas mixture of oxygen and isoflurane for small animal MRI. In the course of these live-animal MRI studies, we observed a Phrygian cap appearance to the gallbladder of one healthy-appearing 6-week-old male mouse, similar to that of the human gallbladder described in many reports. After euthanasia for measurement of bile content, this mouse's gallbladder appeared anatomically normal. To our knowledge, this is the first report of a Phrygian cap appearance of the murine gallbladder.

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31. Quantitative Assessment of an Obstructive Sleep Apnea Patient Before and After Tracheostomy: A Case Study

Obstructive sleep apnea (OSA) can cause severe, debilitating sleepiness and is a well known risk factor for cardiovascular disease. Continued positive airway pressure (PAP) is usually accepted to be the first line medical management in most adults. Some patients with obstructive sleep apnea who do not improve or cannot tolerate PAP therapy may be candidates for surgical intervention. Tracheostomies were performed in the late 1960's to early 1980's as the main surgical therapy for obstructive sleep apnea, until palatal oropharyngeal, hypopharyngeal and facial skeletal surgeries were developed.

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32. Review of Characteristics of Post-Accident Waste Generated in Fukushima Daiichi Nuclear Power Plant Site and Issues to be Addressed in Processing and Disposal Stages

The accident at Tokyo Electric Power Company's Fukushima Daiichi Nuclear Power Station has produced and will continue to produce various types and large amounts of waste contaminated by radionuclides. The literature and published internet information on possible types of waste produced are reviewed from the viewpoint of their characteristics. Issues associated with the waste were selected and analyzed for each stage of the future waste management, considering the characteristics and properties of the waste obtained so far. The stages considered are current (temporary) storage, processing including decontamination and solidification/packaging, storage up to disposal, transportation, and disposal. The issues that should be considered in the safe disposal of waste were extracted as basic information to be used to establish a research and development roadmap. Also the possible resolution of some issues was examined from the experiences of national radioactive waste management and major accidents around the world, i.e., the Three Mile Island Unit 2 accident and the Chernobyl accident. The basic technical information and knowledge in the review are given in the hope that it will promote and facilitate the research and development of radioactive waste processing and disposal methods.

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33. A New Estimate of the Average Earth Surface Land Temperature Spanning 1753 to 2011

We report an estimate of the Earth's average land surface temperature for the period 1753 to 2011. To address issues of potential station selection bias, we used a larger sampling of stations than had prior studies. For the period post 1880, our estimate is similar to those previously reported by other groups, although we report smaller uncertainties. The land temperature rise from the 1950s decade to the 2000s decade is 0.90 ± 0.05°C (95% confidence). Both maximum and minimum daily temperatures have increased during the last century. Diurnal variations decreased from 1900 to 1987, and then increased; this increase is significant but not understood. The period of 1753 to 1850 is marked by sudden drops in land surface temperature that are coincident with known volcanism; the response function is approximately 1.5 ± 0.5°C per 100 Tg of atmospheric sulfate. This volcanism, combined with a simple proxy for anthropogenic effects (logarithm of the CO_2 concentration), reproduces much of the variation in the land surface temperature record; the fit is not improved by then addition of a solar forcing term. Thus, for this very simple model, solar forcing does not appear to contribute to the observed global warming of the past 250 years; the entire change can be modeled by a sum of volcanism and a single anthropogenic proxy. The residual variations include interannual and multi-decadal variability very similar to that of the Atlantic Multidecadal Oscillation (AMO).

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34. Influence of Urban Heating on the Global Temperature Land Average using Rural Sites Identified from MODIS Classifications

The effect of urban heating on estimates of global average land surface temperature is studied by applying an urban-rural classification based on MODIS satellite data to the Berkeley Earth temperature dataset compilation of 36,869 sites from 15 different publicly available sources. We compare the distribution of linear temperature trends for these sites to the distribution for a rural subset of 15,594 sites chosen to be distant from all MODIS-identified urban areas. While the trend distributions are broad, with one-third of the stations in the US and worldwide having a negative trend, both distributions show significant warming. Time series of the Earth's average land temperature are estimated using the Berkeley Earth methodology applied to the full dataset and the rural subset; the difference of these is consistent with no urban heating effect over the period 1950 to 2010, with a slope of -0.10 ± 0.24/100 yr (95% confidence).

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35. RNAi: A Promising Approach to Develop Transgenic Plants Against Geminiviruses and Insects

Viruses, especially geminiviruses and insects infect a wide range of economically important crops across the globe. To reduce the losses caused by them, scientists have adopted several genetic engineering methods to develop resistant plants. Among them, RNA silencing based resistance has proven to be a reliable approach. In this review, we focus on RNAi mediated gene silencing approaches against this class of virus and insects. RNA silencing is a complex and conserved defence mechanism utilized by plants and other eukaryotes to protect themselves from aberrant nucleic acids. The use of RNAi provides an environmental friendly approach to generate plants resistant to viruses and insects, which is not possible otherwise.

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36. Cultured Human Keratocytes from the Limbus and Cornea Both Express Epithelial Cytokeratin 3: Possible Mesenchymal-Epithelial Transition

Background: The corneal limbus is the repository of epithelial stem cells (SC) that sustain the turnover of corneal epithelial cells. The limbus stroma contains mesenchymal SC that generates stromal keratocytes. Mesenchymal-epithelial transition is a phenomenon wherein cells of mesenchymal phenotype can transdifferentiate to epithelial phenotype. Our aim was to study whether limbal keratocytes, cytokeratin 3 (CK3) negative, could be induced to transdifferentiate into CK3 positive cells.

Methods: Human keratocytes were isolated from the limbus and cornea of cadaver donors, cultured and evaluated for CD34, CK3 and vimentin expression by immunofluorescence and RTPCR and for keratocan by RT-PCR.

Results: All cells regardless of site expressed vimentin and some also expressed CD34 and CK3. Double immunofluorescence revealed three subpopulations: CK3−/CD34+, CK3+/CD34+ and CK3+/CD34−. Total CD34 cell yield was higher in the limbus with a peak time to confluence (TTC) of more than 30 days. Total CK3 cell yield was greater in the cornea with a peak TTC of less than 30 days. Increasing donor age corresponded to a decreased CD34 yield and an increased CK3 yield. CK3−/CD34+ and CK3+/CD34− cells behaved similarly to total CD34 and CK3 cells in relation to age, site and TTC while CK3+/CD34+ cells showed intermediate features. Keratocan was present in corneal samples.

Conclusion: Suspension cultured human keratocytes of the limbus behave as progenitor cells of corneal keratocytes being slower cycling and with a greater proportion expressing CD34. Cultured keratocytes both from the limbus and cornea are able to express CK3. This phenomenon may reflect mesenchymalepithelial transition or, given the loss in vitro of the micro-anatomical features of the limbal-corneal area, may indicate the acquisition by keratocytes of a differentiation and migration pathway similar to that of the overlying epithelium. This suggests that the limbus/ corneal stromal niche may exhibit site-specific modulating abilities that direct the development of site-dependent intermediate filament repertoire of epithelial cells.

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37. Hemorrhage into Synovial Cysts as a Cause of Acute Radicular Symptoms: Report of Seven Cases and Review of the Literature

Objective: Acute hemorrhagic synovial cysts are frequently misdiagnosed because the entity is rare. The purpose of is this article to provide insight on the clinical presentation, diagnosis and surgical treatment of this condition.

Summary of background data: Twenty-nine cases reported in the literature were reviewed and presented in this article.

Methods: We retrospectively reviewed seven patients with MRI and exam correlated lesions that underwent resection of a synovial cyst. All patients had acute onset of symptoms, defined as less than three months, and all patients had radiographic and histopathologic evidence of hemorrhage into a synovial cyst. Presenting symptoms included paresthesias, motor loss, or pain in the distribution correlating to MRI location of the lesion.

Results: All patients showed improvement on physical exam and reduced pain. No patients required further surgical intervention during the follow-up period.

Conclusion: Synovial cyst hemorrhage was associated with a rapid clinical course and progression to surgery because of failure of non-operative modalities. Prompt diagnosis and surgical intervention leads to improved outcomes.

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39. Validation of the STOPBANG Questionnaire among Patients Referred for Suspected Obstructive Sleep Apnea

Background: The STOP-BANG is a simple obstructive sleep apnea (OSA) screening tool, part questionnaire (STOP) and part demographic or physical measures (BANG), developed for use in preoperative surgical clinics. This study assessed sensitivity and specificity of the instrument among patients referred to a sleep disorders laboratory, and also its performance characteristics when BANG physical measures are patient-reported rather than measured.

Methods: Adults referred for diagnostic polysomnography completed the STOP questions and answered four yes/no questions (BANG self-reported) about their body mass index (weight and height), age, neck circumference, and gender, which were also assessed by laboratory technologists (BANG-measured).

Results: Among N=219 subjects (mean age 46.3 ± 13.9 [s.d.] years; 98 [44.8%] males) the sensitivity of the STOP-BANG measured for an apnea/hypopnea index (AHI, events per hour of sleep) >5, >15, and >30 was 82, 93, and 97% respectively. Corresponding negative predictive values were 44, 87, and 96%. Specificities were comparatively low (48, 40, and 33%). The STOP-BANG measured and STOP-BANG self-reported scores showed essentially equivalent test characteristics against polysomnography.

Conclusions: The STOP-BANG appears to have limited utility in a referred, sleep laboratory setting. Negative results help to identify some individuals as unlikely to have moderate-to-severe apnea, and may thereby prove useful in identification of patients who would benefit more from laboratory studies than home studies. A STOPBANG in which all information is self-reported may be as effective as the original version, and has potential to facilitate research or community screening where good negative predictive value is required for an effective screening tool.

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40. Human Hepatocellular Carcinoma Metabolism: Imaging by Hyperpolarized ^{13}C Magnetic Resonance Spectroscopy

Purpose: Most cancers exhibit high levels of aerobic glycolytic metabolism with diminished levels of mitochondrial oxidative phosphorylation even in the presence of normal or near-normal levels of oxygen ("Warburg effect"). However, technical challenges have limited the development of non-invasive *in vivo* imaging techniques for monitoring glycolytic metabolism of hepatocellular carcinoma (HCC) and quantitatively evaluating the impact of this effect on the growth and therapy of this disease. Thus, there is a critical need to develop non-invasive techniques for longitudinal assessment of the metabolism and treatment response of patients with unresectable HCCs.

Procedures: This article discusses a novel method, "Hyperpolarized ^{13}C MRS imaging", for achieving this objective and thus improving the prognosis of HCC patients. The primary objective has been to characterize *in vivo* metabolic biomarkers as determinants of HCC metabolism and treatment response of unresectable HCC tumors or viable HCC cells.

Results: This innovative technique capitalizes on a new technology that increases the sensitivity of MRS detection of crucial metabolites in cancer cells.

Conclusion: It is anticipated that this innovative approach will lead to improved methods, both for the diagnosis and staging of HCCs and for the facilitation of the development of enzyme targeted therapies and other therapeutic interventions.

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41. Within-Season Variation of Fitness in Elite Youth Female Soccer Players

Study Background: The within-season variation in fitness measures of elite youth female soccer players (<18 years of age) has not been investigated previously. Further knowledge of this area could allow more effective periodization of training, whilst also enabling coaches to design appropriate long-term athlete development models. This study investigated the within-season variation of fitness test performance in elite youth female soccer players.

Methods: Nineteen elite youth female soccer players aged 11-14 from two age group soccer teams (under 13 (U13) [n=10] and under 15 (U15) [n=9] corresponding to year of birth) participated in this study. A within-players design was used to investigate the variation of selected fitness parameters. The players completed a fitness testing protocol pre-, mid- and post-season, which tested 5 m acceleration, 20 m sprint, repeated-sprint (RSA) and change-of-directional (CoD) performance. Test-retest reliability for these tests was also investigated.

Results: Substantial performance decrements were observed in 5 m acceleration, 20 m sprint and CoD performance at both mid- and post-season when compared to pre-season, with greatest decrements observed in the U13 players. For both groups the most substantial decrements were observed in CoD Performance (6.9 and 10.1% for U13 and U15s, respectively), and 5 m acceleration (8.0 and 3.6% for U13 and U15s, respectively) performance at the mid-season point. RSA was improved post-season in the U13s in comparison to pre- and mid-season. Test-retest reliability for the 20 m sprint, CoD and RSA tests was satisfactory (r>0.68), the 5 m acceleration test demonstrated poor reliability (r=0.24).

Conclusion: In elite youth female soccer players, acceleration, sprint and CoD performance decreased over the course of a season, whilst RSA performance improved in U13 players. Coaches should consider the impact of physiological preparation on performance when working with youth female soccer players, implementing training interventions and recovery strategies accordingly to prevent reduced performance capacity during competition.

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42. Implications of Hemodialysis in Patients Undergoing Coronary Artery Bypass Grafting

Background: Cardiovascular disease is the leading cause of morbidity and mortality in patients on hemodialysis. To our knowledge, no studies have examined long-term outcomes of hemodialysis patients following coronary artery bypass grafting (CABG) in a predominately rural, low-income, and racially dichotomous population

Methods: Long-term survival of hemodialysis patients undergoing non-emergent, isolated CABG was compared with non-hemodialysis patients. Survival probabilities were computed using the Kaplan-Meier product limit method and stratified by hemodialysis. Hazard ratios (HR) and 95% confidence intervals (95% CI) were computed using a Cox regression model.

Results: Hemodialysis patients (n=220) had shorter long-term survival than non-hemodialysis patients (median survival=3.3 versus 14 years, $p<0.0001$). The survival difference remained statistically significant after adjusting for clinically relevant variables (HR=5.2, 95% CI=4.4-6.2).

Conclusion: Hemodialysis Patients generally have an unfavorable outcome after CABG. Further research is needed to address the cost and policy implications of our findings, especially among priority populations.

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43. A Structured Approach for Treatment of Prolonged Cardiac Arrest Cases in the Coronary Catheterization Laboratory Using Mechanical Chest Compressions

Background: This article aims at describing a logistic approach for prolonged resuscitation efforts in the cath-lab using mechanical chest compressions (MCC) during simultaneous percutaneous coronary intervention (PCI).

Methods: When analysing physiological measurements and logistics in 10 patients experiencing prolonged CA in the coronary intervention laboratory (cath-lab), critical areas for improvement were identified. 1. Understanding and commitment to team work with designated individual roles. 2. Practical simulations within the cath-lab setting. 3. Knowledge of the physiological parameters limitations for successful restoration of spontaneous circulation (ROSC). 4. Familiarity with the advanced technology needed.

Results: The medical emergency team and the cath-lab team were trained as one team. A structured approach was developed: In patients not obtaining ROSC following a few minutes of advanced life support according to guidelines, perform MCC during simultaneous PCI and optimize physiological parameters; arterial blood pressure ≥ 70/40 mmHg, end-tidal carbon dioxide ≥ 15 mmHg/2.0 kPa, pulse oximetry >80%, thrombolysis in myocardial infarction-3-flow in open vessels and cerebral oximetry ~45%. Optimization can be done by repositioning the MCC-device, changing the ventilation rate, by use of vasoactive drugs and correction of acidosis. In shock resistant ventricular fibrillation, maintain circulation by MCC until restoration of coronary flow prior to further defibrillation attempts. Consider therapeutic hypothermia.

Conclusion: Implementing a structured resuscitation approach during prolonged resuscitation efforts in the cath-lab, might improve team work and physiological parameters, which may result in a more calm and success-oriented setting.

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44. Using Nano-Arrayed Structures in Sol-Gel Derived Mn^{2+} Doped Tio_2 for High Sensitivity Urea Biosensor

Ordered and self-organized nano-array structures have been developed by Mn^{2+} doping in TiO_2 thin films deposition on conducting substrates by dip coating technique. Mn doped TiO_2 thin films exhibits better bioactivity for enzyme immobilization and cyclic voltammetry measurement has been used for qualitative characterization of electrochemical induction of oxidation-reduction process in TiO_2 and Mn doped TiO_2 films. Due to presence of Mn^{2+} ions at film surface, current voltage characteristic of Mn doped TiO_2 matrix was enhanced by a factor of ten and it had also reduced the crystallite size and promoted transformation of anatase to rutile phase of TiO_2. Urea concentration in the electrolyte was determined by observing chronoamperometry response on urease immobilized working electrodes. The urea detection sensitivity of the Mn doped TiO_2 thin films base platform was 2.3 μA mM-1 cm-2 which is about 15 times higher from only TiO_2 base platforms. Such kind of enzyme–TiO_2/Mnnano-array electrode could contribute a potential prospect in low cost biomedical diagnosis.

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45. Fiber Optic Biosensor for the Detection of Cd in Milk

A novel absorption-transmission based, miniaturized fi ber optic biosensor has been developed for the detection of cadmium in milk. Biosensor constitutes *Bacillus badius* whole cells with phenol red as an indicator co-immobilized onto circular plastic discs with sol-gel approach and a fiber optic transducer system. Inhibition of urease enzyme by cadmium ion has been used as bioassay principle in the study. The detection limit of 0.1 μg/l has been achieved. Sample volume could be miniaturized to 10 μl; miniaturization of sample volume to this level has never been cited in literature. Storage stability of biocomponent was found to be more than 90 days when stored at 4°C in 10% glycerol. Conclusively the study resulted in development of a quick, reliable, miniaturized biosensor with lower detection limit and longer storage stability.

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46. Discerning Data Analysis Methods to Clarify Agonistic/Antagonistic Actions on the Ion Flux Assay of Ligand-Gated Ionotropic Glutamate Receptor on Engineered Post-Synapse Model Cells

Cell-based experiments provide the efficacy of chemicals through the biological function. The authors have described post-synapse model cell-based assay based on qualified analysis for neural drug discoveries. However, in general, cell-based assays often include data fluctuation. This may be a barrier preventing the performance for various practical purposes. In this study, we tried discerning data analysis for clarify the chemical action to the ionotoropic glutamate receptor (GluR), whereby an ion-flux assay of post-synapse model cells is performed and are analyzed based on a chemometrics approach. The dynamic behavior of the GluR of post-synapse model cell was assayed with multivariate data analysis methods namely hierarchical cluster analysis (HCA) and principal component analysis (PCA). By using HCA, we can identify and remove the non-responding samples. By using PCA, the effect of chemicals on the dynamic behavior of ion flux through GluR can be recognized clearly; as either agonist or antagonist. As shown in the results, the GluR-based assay by post-synapse model cell with data analysis methods provide a sodium influx profile which is derived by an agonists or antagonists application. By employing the data analysis methods, PCA and HCA, it is possible to develop a smart cellular biosensing system for qualified analysis.

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47. Unique Cytokine/Chemokine Signatures for HIV-1 and HCV Mono-infection versus Co-infection as Determined by the Luminex® Analyses

Liver disease caused by HIV-1/HCV co-infection is characterized by the inflammation and cell-death. The coexistence of these two chronic viral infections also alters the cytokine production *in vivo*. The ability to visualize changes in cytokine networks with the onset and progression of disease or treatment is critical to advance our understanding of the immune response to pathogens. The recent Luminex® technology has revolutionized the simultaneous detection and quantitation of several cytokines and chemokines in clinical samples that are generally available in small quantities. We have applied this technology to analyze the plasma samples from patients who have either HIV-1 or HCV mono-infection or HIV-1/HCV co-infection and monitored the presence of 23 cytokines and chemokines. Of these, 8 (IFN-α2, IL-2, IL-3, IL-6, IL-8, IL-12p70, IL-15 and RANTES) cytokines were expressed at higher levels in the co-infected individuals. Interestingly, in case of HIV-1 mono-infected individuals, the levels of the proinflammatory cytokines IFN-γ and TNF-α were increased. Standard correlation clustering of the normalized data demonstrated unique plasma cytokine signatures for HIV-1/HCV co-infected individuals. These signatures were characterized not only by an up regulation of the aforementioned antiviral mediators but also by a marked down regulation in the chemokinesEotaxin and MIP-1α when compared to mono-infected individuals. Luminex®-based analyses have proven to be a powerful tool for therapeutic immunomonitoring, but may have an even greater impact in the discovery of the underlying immune response at all phases of infection. The study presented herein has potential to offer insight into the underlying mechanisms of immunopathogenesis of HIV-1/HCV co-infection.

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48. EDDR1 is a Potential Immunotherapeutic Antigen in Ovarian, Breast, and Prostate Cancer

Selection of suitable antigens, preferably targets for cell mediated and humoral immune response is a critical step in the development of cancer vaccines. Cell surface proteins that are over-expressed in cancer cells thus constitute a very attractive class of antigens that can be targeted for effective cancer immunotherapy. Toward this goal, we characterized the relevance of Epithelial Discoidin Domain Receptor 1 (EDDR1) for such targeted therapeutics. EDDR1, a membrane expressed protein associated with adhesion, has recently emerged as a new therapeutic target in several tumor types. In the present study, we analyzed the expression profile of EDDR1 in a variety of normal and cancer cells of human origin by flow cytometry as well as immunohistochemistry. EDDR1 was found to be abundantly expressed on the surface of ovarian, prostate and breast cancer cells but not on the normal counterparts, making it a suitable candidate for antibody mediated therapy. Furthermore, a Human Leukocyte Antigen (HLA) A2-restricted epitope derived from EDDR1 was efficiently presented by various cancer cells to EDDR1 epitope-specific T cells. Collectively, our data present evidence that EDDR1 could be a potential target antigen for immunotherapy.

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49. Th2 Cytokines and Atopic Dermatitis

Atopic dermatitis (AD), a chronic relapsing inflammatory skin disease, is increasing in prevalence around the world. Intensive research is ongoing to understand the mechanisms involved in the development of AD and offer new treatment options for patients suffering from AD. In this review, we highlight the importance of allergic Th2 responses in the development of the disease and summarize relevant literature, including genetic studies, studies of human skin and mechanistic studies on keratinocytes and mouse models of AD. We discuss the importance of the skin barrier and review recent findings on the pro-Th2 cytokines TSLP, IL-25, and IL-33, notably their ability to polarize dendritic cells and promote Th2 responses. After a brief update on the contribution of different T-cell subsets to AD, we focus on Th2 cells and the respective contributions of each of the Th2 cytokines (IL-4, IL-13, IL-5, IL-31, and IL-10) to AD. We conclude with a brief discussion of the current gaps in our knowledge and technical limitations.

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50. Validation of Different Systems for TumstatinExpression and its *in-vitro* and *in-vivo* Activities

The aim of the present study is to identify an effectiveand efficient expression system for purification of recombinantantiangiogenic protein tumstatin. The sequence encodingcarboxy-terminal non-collagenous domain of α3 chain Type IV collagen, α3(IV)NC1 (tumstatin) was isolatedfrom human placental tissue and cloned in three differentexpression vectors pET22b, pcBFT and pAcHLTAto express it in bacteria, mammalian and *Sf-9* insectcells respectively. Expression and purification profiles oftumstatin were evaluated by coomassie staining andimmunoblotting, and the efficiency was determined basedon the yields of soluble protein. Our results indicate that,baculovirus expression system was efficient for scalableyields of soluble protein that could be purified in its biologicallyactive form. This baculovirus expressed tumstatin wasused to evaluate its anti-angiogenic and anti-tumarogenicfunctions such as inhibition of endothelial cell proliferation,cell viability, migration, tube formation, cap dependent proteintranslation and the associated signaling mechanismincluding *in-vivo* tumor study. Our evaluated approachesusing a modified baculovirus expression system shows highexpression and high yield of biologically active tumstatin,as compared to two expression systems, indicatingbaculovirus expression system to be an ideal method forbulk production of soluble tumstatin that needed for preclinicaland clinical trails.

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51. Regrowth Concentration Zero (RC0) as Complementary EndpointParameter to Evaluate Compound Candidates DuringPreclinical Drug Development for Cancer Treatment

The screening process for potential anticancer drugs involvesexpensive and time consuming preclinical and clinicaltrials (CT) before a drug is approved for clinical use(CU). At present, there is a "bottleneck" at the CT/CUtransition because many drugs that showed promising resultsduring preclinical research did not pass clinical trials.We speculated that the endpoint parameters (the inhibitoryconcentration 50 (IC_{50}) or lethal concentration100 (CL100)) commonly used in proliferation assays forshort-term periods (24-72 h) are not useful to predict theantiproliferative effect *in vivo*, especially during clinicaltrials. We propose the use of a parameter, regrowth concentration0 (RC0), which will define the concentration and time necessary to kill 100% of the cells and preventregrowth when drug is removed. The RC0 might introducea new bottleneck at the preclinical stage, "preclinical bottleneck", that will select for drugs with more chances to passclinical trials and improve the success rate of anticancerscreening programs. Our proposal is supported by experimentsdone with the DBTRG-05MG human glioma celllines exposed to short and long-term incubation with threedifferent DNA replication inhibitors (aphidicolin, hydroxyureaand etoposide) and retrospective analysis of clinicaltrials for these drugs.

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52. Model-Based Background Correction (MBCB): RMethods and GUI for Illumina Bead-array Data

IlluminaBeadArray platform (Illumina Inc.)is playing an increasing role in cancer research. MBCB,an R package designed for use on Illumina Bead-Arraydata, allows for microarray data to be pre-processedthrough various model-based statistical methods. Thesemodel-based background-correction methods have provento be a significant improvement over the traditional methodsprovided by Illumina in their BeadStudio software.MBCB accepts the summarized bead-type data; the datacan then be normalized and background-corrected in a statistically-efficient manner. When compared to the popularRobust multi-array (RMA) background correction approachand the default, Illumina-provided background-correctionmethod, MBCB has shown to lead to more precise determinationof gene expression and better biological interpretationof IlluminaBeadArray data. The software developedwill facilitate molecular biomedical-especially cancer-research.

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53. Management of Cutaneous Toxicity and Radiation Dermatitis inPatients with Squamous Cancer of the Head and Neck UndergoingConcurrent Treatment with Cetuximab and Radiotherapy

Skin toxicity is the most common adverse eventassociated with the use of EGFR inhibitors. Radiationdermatitis occurs to some degree in most of the patientswho receive radiotherapy, either alone or in combinationwith EGFR inhibitors. The effects of both toxicities mightbe additive because the irradiated skin zone in squamouscell cancer of the head and neck (SCCHN) patients is thesame area in which the EGFR inhibitor-related acne-likerash is more common. This article summarizes theprincipal issues discussed during a symposium that tookplace in Madrid in January 2009, in which the managementof cutaneous toxicity and radiation dermatitis in patientswith SCCHN was reviewed. Selection of the mostappropriate control measures was discussed in aninteractive debate with the audience using five case reports.It was concluded that early establishment of adequatepreventive measures and proper management of both theEGFR inhibitor-related, acne-like rash and radiationdermatitis in SCCHN patients undergoing concomitanttreatment will prevent treatment interruption, potentiallyallowing better locoregional control of the disease.

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54. Cloudiness and Breast Cancer

Traditional risk factors for breast cancer explain only afraction of cases. Causes for trends in breast cancer incidenceare not fully understood. Breast cancer incidenceand mortality rates decrease with environmental conditionsthat promote Vitamin D synthesis in human skin includinglower latitude and higher personal exposure to sunlight.Association of temporal variability in breast cancer incidencewith changes in cloudiness, which decrease humanVitamin D synthesis is investigated. Association betweentemporal changes in breast cancer incidence and in theautumn cloudiness for preceding years is computed usingdata for the United States. There is a correlation of 0.96(95%CI=0.92-1) between the time series of breast cancerincidence in the age group of 70-79 years and the averagecloudiness in October during preceding 20 years. An empiricalmodel for breast cancer incidence using autumncloudiness in preceding years captures a rapid increase inbreast cancer incidence in the 1980s and some of its yearto-year variability. Increased autumn cloudiness is associatedwith increased subsequent breast cancer incidence. Proposed mechanism includes blocking of solar ultravioletradiation by thick clouds and decreasing the synthesis ofVitamin D in human skin. The findings suggest a newconnection between climate variability and human health.

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55. 3D Volumetric Visualization with Automatic Rigidand Deformable Hybrid Image Registrationfor Adaptive Radiotherapy

To provide more clinically convenient image fusions foradaptive radiotherapy (ART), an automatic rigid and deformableimage registration framework (AIRF) is developedfor multimodal visualization of multiple chronologicalimages and multiple radiotherapy (RT) plans. Our hybridimage registration framework, AIRF, uses a faster but lessaccurate rigid registration method to provide an initial registration,followed by a slower but more accurate deformableregistration method to fine tune the final registration.A multi-resolution approach is also employed in the imageregistration process to further improve the registration accuracy,robustness and efficiency. Volume visualization isprovided to guide the automatic image registration processbecause it can reduce the global positioning error that resultsfrom a partial 3D visual presentation in the three conventionalorthogonal planar views (axial, sagittal, and coronal).The AIRF can automatically align multiple volumetricimages of patients taken over an extended period oftime and can merge multiple radiotherapy plans based ondifferent planning computed tomography (CT) images. Itoffers illustrative 3D volumetric visualization, hybrid rigidand deformable image registration, and automatic transferof RT dose distribution and RT structure models such astreatment targets and organs at risk (OARs) onto chronologicalimages. The AIRF can automatically register multiplevolumetric image datasets of patients taken over anextended period of time and can merge multiple RT plansbased on different planning CT images for 4D or adaptiveradiotherapy.

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56. Characterization of Osteopontin Binding Kineticsin MDA-MB231 Breast and SK-Hep-1 Liver Cancer Cells

Osteopontin (OPN) is a secreted phosphoprotein whichplays a critical role in metastasis of colon, liver, and breastcancers. The canonical pathway for OPN signaling focuseson its binding interactions with integrin and CD44 cellsurface receptors. However, the binding characteristics ofOPN to integrin and CD44 receptors has not been previously examined. In this paper, using MDA-MB231 breastcancer and SK-Hep-1 liver cancer cells, we determine the relative binding characteristics of the OPN ligand to itsintegrin and CD44 cell surface receptors. The apparent KD's for binding to CD44 was 56 μM and 49 μM and tointegrin was 18 μM and 17 μM, in SK-Hep-1 and MDAMB231,respectively. The CD44/Integrin ratio of OPN bound was 1.3 and 3.8 in SK-Hep-1 and MDA-MB231, respectively. Our results indicate that OPN binds to it recognized receptors with substantially different affinities,receptor expression varies between cell types, and significant OPN cell surface interactions that are integrin-andCD44-independent. These uncharacterized interactions may reveal important insights into OPN's role in cancermetastasis.

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57. Saracatinib Impairs Head and Neck Squamous CellCarcinoma Invasion by Disrupting Invadopodia Function

Elevated Src kinase activity is linked to the progressionof solid tumors, including head and neck squamous cellcarcinoma (HNSCC). Src regulates HNSCC proliferationand tumor invasion, with the Src-targeted small moleculeinhibitor saracatinib displaying potent anti-invasive effects in preclinical studies. However, the pro-invasive cellularmechanism(s) perturbed by saracatinib are unclear. Theanti-proliferative and anti-invasive effects of saracatinibon HNSCC cell lines were therefore investigated in preclinicalcell and mouse model systems. Saracatinib treatmentinhibited growth, cell cycle progression and transwellMatrigel invasion in HNSCC cell lines. Dose-dependentdecreases in Src activation and phosphorylation of the invasion-associated substrates focal adhesion kinase, p130CAS and cortactin were also observed. While saracatinibdid not significantly impact HNSCC tumor growth in amouse orthotopic model of tongue squamous cell carcinoma,impaired perineural invasion and cervical lymphnode metastasis was observed. Accordingly, saracatinibtreatment displayed a dose-dependent inhibitory effect oninvadopodia formation, extracellular matrix degradationand matrix metalloprotease 9 activation. These resultssuggest that inhibition of Src kinase by saracatinib impairsthe pro-invasive activity of HNSCC by inhibitingSrc substrate phosphorylation important for invadopodiaformation and associated matrix metalloprotease activity.

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58. Induction of Differential Growth in vitro byHigh-risk Human Papillomavirus in Human BreastCancer Cell Lines is Associated with Caspase Dysregulation

Introduction: Many viruses have been associated with human breastcancers, including Epstein-Barr and Cytomegalovirus.New evidence has revealed the frequent presence of highriskhuman papillomavirus (HPV) strains HPV16 andHPV18 in breast carcinoma biopsies. These findings raisethe question of whether HPV may infect developing cancersand mediate their growth and development, as wasrecently observed with oral cancers. The goal of this studyis to test the hypothesis that these high-risk HPV strainsare sufficient to significantly alter phenotypes of alreadytransformed human breast cancer cell lines.

Materials and methods: A series of *in vitro* experiments, including proliferation,adhesion and viability assays, were used to quantify theeffects of HPV16 and HPV18 on the human breast cancercell lines, T-47D and MCF7, following transient transfectionwith the full length HPV virus. Normal breast andfibroblast cell lines, MCF10A and Hs27, were used as noncancerous controls.

Results: HPV16 and HPV18 significantly inhibited proliferationand adhesion of T-47D cells, although viability was notaffected. Differential effects on proliferation were observedin MCF7 cells; HPV16 inhibited proliferation,while HPV18 stimulated proliferation. No measurableeffects in adhesion or viability in MCF7 cells were observed.The phenotypic changes in T-47D and MCF7 cellswere associated with changes in mRNA expression ofcaspase-2,-3 and -8, but not p53 or GAPDH. No measurablechanges in proliferation or viability were observedfollowing HPV transfection in the normal human breastcell line, MCF10A, or the normal human fibroblast cell line, Hs27, although adhesion was differentially affected.

Conclusions: Although HPV is a primary cause of virtually all cervicalcancers, it is found as a concomitant infection in manyother tumors. While HPV may initiate carcinogenesis in these tumors, recent studies suggest HPV may also modulatethe progression or malignancy process in already transformedcancers. Determining what effects HPV has onalready transformed breast cancers may therefore becomean important step towards understanding the factors thatwill lead to more effective treatment options for a significantproportion of breast cancer patients.

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59. Oral Submucous Fibrosis: Review on Etiopathogenesis

Summary data from recent epidemiological studies provideoverwhelming evidence that areca nut is the mainaetiological factor for OSF. Commercially freeze driedproducts such as pan masala, Guthka and mawa have highconcentrates of areca nut per chew and appear to causeOSF more rapidly than by self prepared conventional betelquid that contain smaller amounts of areca nut. It islogical to hypothesize that the increased collagen synthesisor reduced collagen degradation as possible mechanismsin the development of the disease. These chemicalsappear to interfere with the molecular processes of depositionand/or degradation of extracellular matrix moleculessuch as collagen. In vitro studies on human fibroblastsusing areca extracts or chemically purified arecoline supportthe theory of fibroblastic proliferation and increasedcollagen formation that is also demonstrable histologicallyin human OSF tissues. The copper content of areca nut ishigh and the possible role of copper as a mediator of fibrosisis supported by the demonstration of up regulationof lysyl oxidase in OSF biopsies. It has been postulatedthat areca nut may also induce the development of thedisease by increased levels of cytokines in the lamina propria.Current evidence implicates collagen-related genesin the susceptibility and pathogenesis of OSF. The individualmechanisms operating at various stages of the disease–initial, intermediate and advanced–need further studyin order to propose appropriate therapeutic interventions.

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60. Non-Thermal Effects of Far-Infrared Ray (FIR) on HumanHepatocellular Carcinoma Cells HepG2 and their Tumors

Background: We developed a cell culture CO_2 incubator and a mice rack that can continuously irradiate cells or murine with FIR. Our goal is to make clear the non-thermal effect of FIR on HepG2 with these instruments morphologically.

Methods: By using them, *in vitro*, we examined theproliferation of cultured HepG2 cells with hematocytometer, BrdU assay, WST-1 assay, HE staining, Toluidine bluestaining and microarray studies. And *in vivo*, we measuredthe tumors, observed the sections by IHC, DAPI stainingwith light microscopes and performed microarray studies.

Results: Proliferation of HepG2 cells were suppressed (e.g., cell count declined by 34% after 10 days of FIRirradiation), tumor volumes reduced by 86% after 30 daysof FIR irradiation, mRNA of Vascular Endothelial GrowthFactor (VEGF) decreased by 48%, vascular area in crosssections from the tumors decreased 60% compared withthe control. More frequent properties in apoptosis wereobserved by TUNEL and DAPI staining in FIR-treatedgroups. Body weight of mice increased compared with thecontrol. Oxydation and Reduction (Redox) reactions by H+ (proton and electron)/O_2- (a kind of Reactive OxygenSpecies (ROS)) were induced by FIR.

Conclusions: These results clarified that FIR inhibited the proliferation of HepG2 at non-thermal circumstances (at 25 ± 0.5, 37 ± 0.5°C). FIR will serve as a tool againstdiseases induced by HepG2.

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61. Clinical Studies on Hormonal Status in Breast Cancerand its Impact on Quality of Life (QOL)

Breast cancer is a steroid hormone–dependent tumor.Stratification of patients according to hormone (ER/ PR)receptor status and nodal metastasis is of great therapeuticimportance. In this investigation, we could enroll 79pre and post-menopausal breast cancer patients voluntarily. We classified these cases into four categories of thecombinations of ER/PR positive, negative and mixed statuses.Their hormone receptor status as determined byimmunohistochemistry correlated with therapy regimenslike chemotherapy, hormone therapy and QOL responses.We found that in ER+/PR- and ER-/PR- tumors were morefrequent in postmenopausal women than ER+/PR+ tumors.The ER+/PR- tumors were larger than ER+/PR+ tumors. Inaddition, 21.51% of ER+/PR- and 17.72% of ER-/PR- patientshad four or more axillary nodes involved with tumorscompared to patients with ER+/PR+ tumors (7.59%).Postmenopausal women with ER+/PR- and ER-/PR- whoreceived adjuvant hormonal therapy or combination ofchemo drugs like Cyclophosphamide, Adriamycin, 5-FU(FAC) and Cyclophosphamide, Alurubicin, 5-FU (CAF)showed good response than premenopausal women. Fortypatients receiving tamoxifen (hormone therapy) along withother chemo- drugs also showed good response. Tamoxifeninduced substantial tumor regression and increased diseasefree survival. It is concluded that hormone receptorstatus is important in deciding the choice of treatment forall subgroups and influenced the QOL. Another significantobservation was that the frequency of ER+/PR- andER-/PR- tumors was higher in this study group compared to ER+/PR+ tumors. This is the first report from south Indianpopulation indicating the importance of hormonalstatus in deciding therapeutic regimens in breast cancerpatients affecting their QOL.

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62. Genes Encoding Enzymatic Activities Implicated in theEicosanoid Cascade of Arachidonic Acid and their Receptorsare Expressed at mRNA Levels in Human Meningiomas

In view of the important oncogenic action of lipoxygenase(LOX) and cycloxygenase (COX) enzymatic activities weinvestigated, by using real time PCR, their presence in humanmeningiomas. Results indicated the presence of 5-LOX,12-LOX, 15-LOX1, 15-LOX2, COX-1, COX-2, prostaglandin E (PGE) synthase, prostacyclin (PGI) synthase andthromboxane (TX) synthase transcripts in meningiomas butwithout relation to the tumor grade, the subtype of meningiomas,the presence of inflammatory infiltrated cells, ofan associated edema, mitosis, brain invasion, vascularisationor necrosis. Similar results were found for BLT1 and BLT2transcripts (encoding LTB4 receptors) and for prostanoidreceptor transcripts (EP1-4 for PGE2, IP for PGI2 and TPfor TXA2). In conclusion, genes encoding enzymatic activitiesimplicated in the eicosanoid cascade are expressedin meningiomas. LOX- and COX-derived arachidonic acidmetabolites might act on tumor growth not only by actingon cell growth but also by altering the local cytokine and/or angiogenic networks.

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63. Larynx Preserving Treatments in the Early andAdvanced Laryngeal Cancers; A Retrospective Analysis

Background: To assess tumor control and survival ofthe patients with laryngeal cancers who receivedchemoradiation or radiotherapy alone as definitive treatment.

Material and methods: Patients with laryngeal cancerswho received organ-saving treatment were enrolled in thistrial.

Results: In 147 cases, chemoradiotherapy was administeredin 61 patients. Twelve cases were excluded from theanalysis because of the treatment interrupt or death. Fiftyeight cases had early-staged disease. In median time of followup (9.9 months), mean overall survival and mean diseasefree survival were 51 months and 37 months in earlylesions, and 30 months and 17 months in locally advancedtumors, respectively. Local control rate was 60% in earlystaged and 43.5% in locally advanced cases. The mean totalradiation dose significantly affected the tumor controlin chemoradiation group.

Conclusion: It seems that radiotherapy or chemoradiationcan be appropriate alternative to total laryngectomy in laryngealcancers.

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64. Characterization of Treatment Response to RecombinantInterferon-α2b in Osteosarcoma Xenografts

Interferons (IFNs) may target cancer cells both throughtheir regulation of the immune response, effect on angiogenesisand through direct effect on cancer cells. Treatmentresponse has been demonstrated in osteosarcoma patients,but tumour resistance to IFN-α is common. Hence,understanding the molecular mechanisms involved in responseand resistance is essential for improving therapeuticefficacy. Of five xenografts screened for specific growthdelay in response to treatment with unconjugated and PEGylated IFN-α2b, one displayed growth inhibition andtumour shrinkage. Growth inhibition increased on a dosingschedule of PEGylated IFN every third day. Xenograftsresistant to PEGylated IFN were similarly resistant tounconjugated IFN. Combination treatment with IFN-α2b and doxorubicin resulted in improved growth control rates. Transcriptional profiling analysis of the one sensitive andtwo resistant xenografts identified a common set of 79 genessignificantly affected by IFN-α2b treatment independentof tumour growth inhibition. All but four of the 79 geneswere up-regulated. The majority of these genes were wellcharacterized IFN-stimulated genes and core members ofthe IFN-α signalling pathway. The expression of a set of 128 unique genes changed only in the sensitive xenograft; 52/128 genes were up-regulated. The specificgeneexpression pattern seen in the responsive xenograftidentified possible pathways important for the antitumoreffect of IFN-α in osteosarcoma, including ssubsets of genesinvolved in cell adhesion and osteogenic tissue development. The observed improved control rates of combinedtreatment with IFN and doxorubicin are encouraging andshould be further explored.

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65. GAssociation of Butyric Acid Produced by PeriodontopathicBacteria with Progression of Oral Cancer

Objective: The association between periodontal diseaseand the risk of various human cancers including oral squamouscell carcinoma (OSCC) has been suggested. Butyricacid (BA), an extracellular metabolite fromperiodontopathic bacteria, plays an important role in theprogression of periodontal disease. Recent studies haveshown that podoplanin, a transmembrane glycoprotein, isexpressed in various normal as well as neoplastic tissues.In this study, the effects of BA/sodium butyrate (NaB) onpodoplanin expression, cell migration and epithelial-mesenchymaltransition in OSCC cell lines were examined.

Methods: Ca9-22, HSC-2, -3 and -4 cells were incubatedwith NaB, and then subjected to real-time RT-PCR,western blotting and scratch assay.

Results: NaB increased the expression of podoplanin inHSC-2 and -3 cells and vimentin in Ca9-22 cells. Cell migrationwas promoted at a low concentration of NaB especiallyin HSC-3 cells, whereas it was inhibited in HSC-2 and -4 cells. Scratch assay of HSC-2, -3 and -4 revealedthat cell migration was markedly inhibited by addition of asiRNA specific for podoplanin.

Conclusion: BA/NaB increases podoplanin expressionand cell migration in certain OSCC cell lines, suggestingthat the progression of periodontal disease may promotethe progression of OSCC via a podoplanin-dependent pathway.

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66. Effect of Y-90 SIR-Spheres Therapy for MultipleLiver Metastases in a Variety of Tumors

Objective: To evaluate the outcomes of patients receiving Y-90 SIR-Spheres in patients with multiple liver metastases fromdifferent tumors.

Methods: 29 consecutive patients with multiple livermetastases from colorectal (13), Islet cell tumors (9), carcinoidtumors (4) or non-small cell lung cancer (3) who were treated with Y-90 SIR-Spheres between March, 2003 and February,2006 were included. Only patients who had follow-upradiological exams at our institution were included. Dataregarding Y-90 SIR-Spheres dose, lobe of liver treated, andchemotherapy (CTx) administered were collected. Patients'outcomes were evaluated based on radiological evidence ofchange in size and number of liver metastases.

Results: The study population included 8 females and 21males at a mean age of 60y. The mean Y-90 SIR-Spheres doseadministered was 39.8 mCi. Both lobes of the liver, the rightlobe only or the left lobe only were treated in 26, 2, 1 patients,respectively. Sixteen patients received Y-90 SIR-Spheres afterCTx failure, 5 patients as adjuvant therapy after completion ofCTx, 7 patients as concurrent therapy and one patient refusedrepeat CTx. The mean interval between the last CTx and Y-90SIR-Spheres was 108 days. Four patients (14%) demonstratedradiological improvement and 9 (31%) were stable for a meaninterval of 2.8 mo. after Y-90 SIR-Spheres infusion. Sixteenpatients (55%) demonstrated continued progress of livermetastases.

Conclusion: Y-90 SIR-Spheres therapy is useful in reducingor stabilizing multiple liver metastases from a variety of tumors.

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67. Endocan as a Biomarker of EndothelialDysfunction in Cancer

Endocan also called endothelial cell-specific-molecule-1is a product of endothelial cells, highly regulated by vascularendothelial growth factor and expressed during the switchbetween dormant to fast-growing angiogenic tumors. Noother molecule is currently known to be a read out of endothelialactivation and dysfunction in tumor progression.We here reviewed the present knowledge about endocanthat present clinical value as a tissue- and blood- basedprognostic and potentially as a companion biomarker incancer. By immunohistochemistry endocan was shown tobe overexpressed into endothelial cells of small and largevessels in lung, kidney and brain tumors. High endocan serum levels were shown to be significantly correlated withthe presence of metastasis and with limited survival in kidneyand lung cancers. Moreover, endocan release by endothelialcells was in vitro modulated by addition of anti-angiogeniccompounds. At a time where biomarkers are hugelyneeded to improve anti-angiogenic targeted treatments,endocan could be a pertinent biomarker to select patientsand/or to clinically monitor the efficacy of cancer drugs.Through its awaited functional applications, endocan appearstoday as a promising biomarker to access to personalizedmedicine and to optimize therapy cost / benefit ratio.

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68. Malignant Fibrous Histiocytoma - An UnusualTransformation from Benign to Malignant

Background: Malignant Fibrous Histiocytoma (MFH)is one of the most common soft tissue sarcoma in adultsand typically arises in the soft tissues of the extremitiesand retroperitoneum. The head and neck region are seldominvolved accounting for 3-8.5% of the cases. In thesuperficial sites such as skin, MFH may behave in a benignfashion despite the high grade appearing and fast growingtumor cells, with a reported incidence of malignanttransformation around 1%.

Case Description: A 72 year old male patient reportedto the Department of Oral Medicine & Radiology with achief complaint of recurrent pain and swelling over the upperlip and nose region which was surgically drained a monthback. This was the third occurrence of the swelling overthe past 13 years. In the past 2 episodes, he was surgicallytreated for Benign Fibrous Histiocytoma (BFH). Surgicalbprocedure and histopathological report confirmed malignant transformation into MFH in the recent episode.

Conclusion and Clinical Implications: This publicationaims to highlight the possibility of malignant transformationof benign fibrous histiocytoma and the importance of longterm followup.

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69. Squamous Cell Carcinoma of the Kidney–Rarity Redefined:Case Series with Review of Literature

Squamous cell carcinoma of the renal pelvis and ureter is a rare malignancy, having an incidence of 6% to 15% (of all urothelial tumors). Few cases of primary squamous cell carcinoma of kidney have been reported in the worldliterature. The insidious onset of symptom and lack of any pathognomonic sign, leads to delay in the diagnosis andsubsequent treatment, resulting in grave prognosis for these patients.Herein, we report 5 cases (three males and two females) of advanced primary squamous cell carcinoma of kidneythat were treated at our centre during the last 6 years. The average age was 57 years (range 50-65 years). Three of thepatients had history of long standing renal calculus disease while 3 had history of smoking and 1 patient had history ofanalgesic abuse. These cases were unique because in few of them; all the calyces were involved by the tumor-a fieldchange type of pattern normally seen in transitional cell carcinoma of the kidney. In one patient, thrombus of the inferiorvena cava was also present along with infiltration of the duodenum by the tumor. Despite prompt nephroureterectomy, 4 out of 5 patients died within 6 months of treatment. Only one patient was surviving at 5 months of follow up.

Nephrectomy with or without ureterectomy is the treatment of choice in patients suffering from squamous cellcarcinoma of the kidney. There is lack of evidence of survival benefits of chemo-radiation following surgery but isadvocated by some with the hope that it might increase survival. Biopsy from the renal pelvis or calyceal wall isadvocated at the time of stone removal in patients having long-standing history of large renal calculi or staghorn calculussince such patients are capable of harboring occult or overt malignancy.

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70. Cheilitis Granulomatosa-An Uncommon ClinicopathologicalEntity: A Case Report

Granulomatous lesions of the Oral and Orophrayngealsubmucosal tissues frequently affecting buccal and labialtissues are uncommon and present a diagnostic dilemma because of the wide variety of possible etiologic factors.The lesion affecting lips initially described by the German dermatologist Miesher as CheilitisGranulomatosa is a raredisorder characterized by non-remissive enlargement of one or both lips.The multiple causes and clinical features of CheilitisGranulomatosa often create a confusing maze through whichthe clinician must carefully proceed in order to develop an accurate diagnosis and provide an effective treatment.Management considerations for these patients depend upon the results of the investigations, patient's esthetic considerations and severity of the condition.This article, besides discussing a successfully treated case of CheilitisGranulomatosa along with gingivalinvolvement in a 27 year old Indian woman, also highlights the importance of differentiating this condition from other lip swellings.

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71. Role of Chemokines and Chemokine Receptors in ProstateCancer Development and Progression

Prostate cancer (PC) is the second leading cause of cancer deaths in men in America and Western Europe.Epidemiological studies suggest that prostate cancer incidence & increased in last few years in Asia. The causesor consequences of increasing trend of prostate cancer incidence are not completely known. Emerging evidencessuggest that among the many risk factors, inflammation is the major risk factor for developing prostate cancer andits progression to metastasis. It is proposed that exposure to environmental factors such as infectious agents, dietaryagents and saturated lipids leads to injury of the prostate due to chronic inflammation and regenerative risk factorlesions referred to as proliferative inflammatory atrophy (PIA). These phenomena predominantly control by a number ofpro-inflammatory macromolecules such as chemokines, and their receptors. Some recent studies suggest that many ofthese pro-inflammatorychemokines and their receptors are the products of protooncogenes in many cancers includingthat of the prostate. This review focus on the current biology of chemokines and chemokine receptors in prostate cancer.An understanding of this axis may enable researchers to develop targeted strategies for prostate cancer.

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72. Relation Between Tumor Size and Range of Motion in IMRTTreatment Planning for Thoracic Lesions

Purpose: To evaluate the relation between tumor size/volume, tumor range of motion, and healthy lung volume inlight of radiotherapy motion management paradigm.

Materials and Methods: Four patient data sets were considered in this investigation. Each patient underwent timeresolved (4D) CT data scan. Mid-ventilation CT data sets, with nominal lung volumes ranging from ~3000 cm3 to ~6000cm3, were considered for treatment planning. Spheres with pre-specified radii were auto-contoured in the left lower lobesas simulated planning target volumes (PTVs) for each patient. Motion in superior-inferior direction was superimposed onthe simulated spherical PTVs, such that motion-inclusive ITVs were generated. Nine-fi eld IMRT treatment plans werecreated for all lung volumes, different combinations of simulated PTV spherical size and ranges of motion. Three doselevels of 60 Gy, 70 Gy, and 80 Gy were utilized. The doses were prescribed to 95% of the ITV. Simulated PTV sizesand ranges of motion were varied until prescriptions were met, given that organs at risk (OARs) were spared. The OARconstraints were: 40 Gy to 1% of the cord and 30% of the heart, as well as 20 Gy and 30 Gy to 30% and 20% of benignlung, respectively. These constraints, representative for 2 Gy per fraction fractionation schemes, are commonly usedclinically. The treatment plans were deemed clinically acceptable when standard deviation of the dose across the ITVwas less than 3% of the prescription dose in addition to fulfillment of the OAR constraints.

Results: For each nominal lung volume three look-up curves, corresponding to the prescription dose levels weregenerated. The plots related the PTV sphere sizes with its range of motion. In addition, correlation between the absolutetumor volume and its range of motion was also established and presented in graphical format.

Conclusions: The motion management threshold of 0.5 cm found in the literature is reasonable. However, in somecases, depending on the tumor size, tumor range of motion, and nominal lung volumes, it might be too restrictive. In thedetermination of the most appropriate individualized treatment planning approach all factors such as tumor and lungvolumes, tumor range of motion and patient tolerance toward the treatment technique need to be assessed.

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73. Are all Glioma Cells Cancer Stem Cells?

The cancer stem cell theory proposes that there is a small but constant subpopulation of cancer cells with stem cellproperties responsible for the self renewal capacity and unlimited proliferation of tumor as well as increased resistanceto antineoplastic drugs. Targeting these cells might constitute an effective way to cure cancer. Regarding gliomas, byanalysing proliferation kinetics of cultures containing mixed subpopulations and experimental data from literature onglioma cell lines, we propose a model (Stemness Phenotype Model) in which all glioma cells have stem cells propertiesbut their phenotype varies depending on the environmental conditions. This model provides an alternative explanationto different and sometimes controversial experimental fi ndings and might be a useful guide for future research in thefi eld of gliomas and stem cell biology.

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74. Activation of Multiple Molecular Mechanisms for IncreasingApoptosis in Human Glioblastoma T98G Xenograft

Glioblastoma is the most malignant brain tumor of astroglial origin. It renders poor response or resistance toexisting therapeutics. We used all-*trans* retinoic acid (ATRA) and interferon gamma (IFN-γ) alone and in combinationfor controlling human glioblastoma T98G xenograft in nude mice. Histopathological examination showed astrocytic differentiation in ATRA group, some apoptosis in IFN-γ group, and occurrence of differentiation and enhancement ofapoptosis in ATRA plus IFN-γ group. ATRA plus IFN-γ induced extrinsic pathway of apoptosis by activation of caspase-8 and cleavage of Bid to tBid and also promoted intrinsic pathway of apoptosis due to down regulation of hTERT, c-IAP2,and survivin and upregulation of Smac/Diablo. Mitochondrial release of apoptosis-inducing factor (AIF) inducedcaspase-independent pathway and also upregulation of calpain and caspase-dependent pathways ultimately activatedcaspase-3 for apoptosis. Increased activities of calpain and caspase-3 degraded 270 kDa α-spectrin at the specifi c sitesto generate 145 kD aspectrin breakdown product (SBDP) and 120 kD SBDP, respectively. *In situ* TUNEL and doubleimmunofluorescentlabelings detected apoptosis with increased expression of calpain, caspase-12, caspase-3, and AIF in tumors after treatment with IFN-γ and most effectively with ATRA plus IFN-γ. Results indicated that ATRA plus IFN-γ activated multiple molecular mechanisms for increasing apoptosis in human glioblastoma *in vivo*.

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75. MTA1 Aids the AKT Pathway by Inhibiting Expression of a Key Regulator, PTEN

Metastasis is the fi nal result of actions of various genes, one of which is the Metastasis Associated 1 (MTA1) gene.MTA1 acts as part of a nucleosome remodeling and histone deacetylation complex and has been shown to aid metastasisby regulating many other molecules. We decided to study if there was any possible relationship between MTA1 andbthe phosphatase and tensin analogue mutated on chromosome 10 (PTEN). PTEN is a tumour suppressor gene knownto be mutated in several cancers. We found that on knockdown of MTA1 using siRNA, PTEN protein levels increasedalbeit its mRNA levels were unchanged. We further found that MTA1 and PTEN colocalize and coimmunoprecipitatewith each other. PTEN levels increased on inhibiting histone deacetyalse activity, such as possessed by MTA1. One ofthe most celebrated functions of PTEN is its regulation of the PI3K-Akt pathway. We found that the levels of active AKTdecreased in cells treated with siRNA against MTA1. We hypothesize that MTA1 helps in maintaining the AKT pathwayin cancer cells by inhibiting PTEN, a major antagonist of the pathway. This might be one of the several mechanisms bywhich MTA1 aids metastasis.

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76. Ovarian Carcinoid Tumor with Nodal Metastases: Case Report

Primary ovarian carcinoid tumors are very rare, they represent less than 0.1% of all ovarian cancers. The insulartype is the most common, followed by the stromal, trabecular and mucinous types. A woman of 47 years old presentedwith lower abdominal pain, ultrasound evaluation revealed a voluminous pelvic mass on the right side. The patientunderwent debulking surgery, it was diagnosed a carcinoid of the left ovary with prevalent trabecular and partlycribriform and insular pattern. Our patient had periaortic lymph node metastases, in this respect there is no evidenceof involvement of lymph nodes for primary ovary, especially in the trabecular form, except for intestinal and pulmonarycarcinoids. Therefore, this is the fi rst case of mixed primary ovarian carcinoid, particularly in predominantly trabecularform, with lymph node metastases, as described in the literature.

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77. Proteolytically-cleaved Fragments of Cell Surface ProteinsStimulate a Cytotoxic Immune Response AgainstTumoractivatedEndothelial Cells *In vitro*

Endothelial antigens that stimulate immune-mediated damage of tumor vessels represent possible targets forthe development of antiangiogenic vaccines aimed at preventing the progression of solid tumors. Since antigensexpressed on the cell surface are accessible targets for both humoral and cell-mediated immune responses, the abilityto isolate extracellular protein fragments from endothelial cells by proteolytic digest is a proposed strategy for thecreation of antiangiogenic vaccines. Human microvascular endothelial cells (HMEC) were isolated from an abdominalsubcutaneous adipose tissue biopsy. Both non-activated endothelial cells (nHMEC) and tumor-activated endothelialcells (aHMEC) were obtained. HMEC lysate and cleaved fragments of cell surface proteins (FCSP) of HMEC had totalprotein concentrations of 135 µg/mL and 2 µg/mL, respectively. Despite this difference in concentration, FCSP wereable to stimulate immune cells in cytotoxicity assays better than the HMEC lysate. Moreover, FCSP obtained fromtumor-activated endothelial cells were able to stimulate an immune response toward tumor-activated endothelial cells.Based on these results, FCSP of endothelial cells appear to provide a comprehensive set of surface antigens that areable to induce targeted, immune-mediated cytotoxic effects against tumor endothelial cells. These fi ndings represent asuccessful strategy to produce safe and pure antigens for the production of antiangiogenic vaccines.

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78. Neoadjuvant Chemotherapy with S-1 for Patients with Oral Squamous Cell Carcinoma

S-1, an oral anticancer drug, is comprised of tegafur (a prodrug of 5-fl uorouracil) and two biochemical modulatorsthat have effect-enhancing and adverse reaction-reducing activities. Neoadjuvant chemotherapy (NAC) using S-1 hasnot been reported. Between April 2003 and March 2008, 103 patients with previously untreated oral squamous cellcarcinoma (OSCC) received some courses of S-1 NAC (S-1 80 mg/m^2/day as the NAC until 1 week preoperatively).Tumor size and histopathologic effect were evaluated before and after treatment. Among 103 cases, 10 cases hadcomplete responses and 53 cases had partial responses (overall response rate [RR], 61.2%). Twenty-two (21.4%) patients had adverse events. Most patients had mild toxicities in the bone marrow and digestive tract (grade 1, 19 cases). Only three patients (2.9%) had grade 2 neutropenia or grade 4 thrombocytopenia. We examined the relationshipbetween the RR and the clinicopathologic behaviors. The RR of the pN2 cases (33.3%) was significantly lower than thatof the pN0 cases (69.4%). The RR was not correlated with tumor size, differentiation type, distant metastasis, and theperiod of administration. The data indicates that S-1 caused only mild toxicity and had highly effective antitumor activity. Furthermore, the RR of S-1 NAC might predict regional lymph node metastasis.

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79. Assessing the Dosimetric Consequence of Inter-fractional Setup Shifts on Helical Tomo Therapy Plans with Independent Dose Calculation

This work studied on dosimetric impact due to inter-fractional uncertainties for one hundred patients from fivedifferent treatment sites (30 prostate, 26 head & neck, 18 lung, 17 pelvis, and 9 brain patients) for Tomotherapy modality.Daily setup shifts were quantified and grouped into systematic (mean daily setup shifts) and random shifts (fractionbasedshifts with corresponding systematic shift subtraction). Both systematic and random shifts were incorporatedinto in-house independent point dose calculation software, MU-Tomo, to separately evaluate the systematic andrandom dosimetric variations. Systematic dosimetric variations showed large dose deviation, with the largest differenceat-10.02% compared to the planned dose and 3% standard deviation. Mean random dosimetric variations showedrelatively small dose deviation with the largest at -5.65% compared to the planned dose and 1.9% standard deviation.Furthermore, different treatment sites were sorted into the head & neck and brain group, and the body group includinglung, pelvis, and prostate cancers. According to ANOVA analyses, random dosimetric variations were found significantlydifferent between patients treated at the same treatment site, while systematic dosimetric variations were significantlydifferent between the head & neck and brain group and the body group. No significant differences were discoveredamong specific patients for systematic dosimetric variations, and no significant differences were observed within eachof the two groups for random dosimetric variations. Dosimetric consequences are not significantly correlated withtreatment fraction number according to the Pearson correlation analysis. By comparing doses without any shift againstthose with the random shift, overall dosimetricimpacts to each patient were found to be very small with the mean value-0.0053% and standard deviation of 1.11%. Ninety-nine percentage of the averaged variation results were within 3.5%.This implies that overall dosimetric impact from random variations is small; instead, dosimetric impact is more affectedby systematic shifts.

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80. *MU-Tomo*: Independent Dose Validation Software for Helical Tomo Therapy

A software program, *MU-Tomo*, has been developed to perform an independent point dose calculation and compareit to the dose calculated from the TomoTherapy (TomoTherapy, Inc., Madison, WI) treatment planning system (TPS).Input parameters required for this software include: archived tomotherapy patient fi les, QA plan image coordinates,tomotherapy-calculated point dose and machine-specifi c dosimetric parameters such as the off-axis ratios (OARx andOARy), tissue phantom ratios (TPR) and output functions (Scp). The software was validated on four phantom models andfi ftytomotherapy patient plans representing various anatomical sites. Our results indicate that *MU-Tomo* can perform ina few seconds an independent dose calculation accurately and provide a secondary check for a point dose validationof helical tomotherapy plans.

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81. Prognostication of Histomorphological Characteristics inMultiple Myeloma

Objective: To study the utility of Bartl´s histological grade and staging in the prognostication of multiple myeloma.

Methods: It was both a retrospective and prospective study done using all the cases of multiple myeloma fromJanuary 2001 to December 2002 with 2 years follow up. These cases were studied with special reference to Plasma cellmorphology, biopsy growth pattern and tumor burden. In addition the effects of chemotherapy on post therapy marrowwere also studied.

Results: During this period we studied 40 cases, of which 34 cases were Marschalko type, 6 cases Plasmablastic.The volume of infiltration, 29 cases showed >50% of volume of infiltration, 3 cases showed 20-50% of volume ofinfiltration and 8 cases showed <20% of volume of infiltration. In the Pattern of involvement, Interstitial+Nodular type of involvement was commonly noted in 18 cases, interstitial type was seen in 15 cases and diffuse type was observed in 7 cases.

Conclusion: Bone marrow aspiration along with trephine biopsy is essential for the diagnosis and management of multiple myeloma.

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82. Docosahexaenoic Acid (DHA) Induces P53-DependentGrowth Inhibition in Transformed Colon and Lung Cell LinesExpressing Wildtype *P53*

Supplementation with n-3 polyunsaturated fatty acids, both in dietary in vivo studies, as well as in vitro tissue culturemodels, has anti-proliferative effects on tumor cells. In the current study, the role of p53-dependent growth inhibitionby docosahexaenoic acid (DHA), an n-3 polyunsaturated fatty acid, is examined. Previous work has established that DHA is capable of growth inhibitory effects independent of p53 mutational status in colon carcinomas, however, one ofthe same studies showed an increase in the number of apoptotic cells (measured by Annexin V-FITC) only in the DHA treated cells of the colon carcinoma with wildtype p53. To determine the potential role of p53 on the growth inhibitionobserved with DHA treatment of the human colon carcinomas COLO-205 (wildtype p53) and WiDr (mutant p53, His 237) and the human lung adenocarcinomas A549 (wildtype p53) and H441 (mutant p53, codon 158), p53-specific siRNA's and a chemical inhibitor of p53, pifithrin-α, were employed in vitro. Significant increases in the number of DHA-treatedcells by p53 siRNA or pifithrin-α addition were observed only in the COLO-205 and A549 cell lines expressing wildtype p53, and these correlated with a reduction in the percentage of apoptotic and necrotic cells. This data confirms a rolefor p53-dependent growth inhibition with DHA treatment.

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84. Neutropenic Enterocolitis as Possible Complication of Docetaxel and Epirubicin Chemotherapy for Breast Cancer:Report of 3 Cases

Neutropenic enterocolitis (typhilitis) is a rare complication ofchemotherapy-related neutropenia in cancer patients (Cunningham et al., 2005; Davila, 2006; Hsu et al., 2006; D'Amato et al., 2006; Ibrahim et al., 2000). Its main clinico-pathologic features include segmentalulceration of the caecum and ascending colon which may progressto necrosis and peritonitis. Its pathogenesis appears to result froma combination of mucosal damage and impaired host defences tointestinal microorganisms (Cunningham et al., 2005; D'Amato et al., 2006). We report on 3 homogeneously treated patients presentingneutropenicenterocolitis following Docetaxel and Epirubicinchemotherapy for advanced breast cancer. In all 3 cases doses were75 mg/m^2 for Docetaxel and 90 mg/m2 for Epirubicin plus prednisonemedication. Treatment was repeated every 3 weeks.

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85. Treatment Couch Modeling in the Treatment Planning SystemEclipse

Purpose: Previously in treatment planning systems (TPS) the treatment couch was expected to be made out ofair-equivalent material due to the used material (Carbon). Some studies have already shown that the treatment couchcannot be neglected during treatment planning. Now a days the manufacturer of TPS implemented the feasibility to insert treatment couch structures. This study aimed to find the correct modeling of the treatment couch parameters in the TPSE clipse.

Method: The Varian Exact Treatment Couch consists of a carbon board (length 2.5 cm) and two moveable rails (length 8.5 cm) underneath. The treatment couch can be modeled in TPS by changing the Hounsfield units (HU) for eachpart of the treatment couch. For low and high photon energies the attenuation of the treatment couch was measured ata Clinac 2300 C/D and in the TPS the attenuation of the treatment couch model was determined for different sets of HU values. Measured and calculated attenuations were compared to each other.

Results: Minimum aberration between the calculated and measured attenuation of treatment couch were found for the HU values of -750 HU for the carbon plate, -995 HU for the filling of the carbon plate and 225 HU for the rails.Additionally it was found that the attenuation is dependent on the gantry angle. Like expected the highest attenuationwas found in the region of the rails underneath the treatment couch.

Conclusion: For Varian Exact Treatment Couch the HU values should be adjusted to -750 HU for the carbon plate, -995 HU for the filling of the carbon plate and 225 HU for the rails. The same HU set can be used for low and high photonenergies. With the correct set of HU values the treatment couch is modeled correctly in the TPS Eclipse.

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86. Exposure to Interferon g Decreases Levels and Activity of Key Cell Cycle Proteins Resulting in Severe Growth Arrest of the Human Non-Transformed Cell Line, WISH

Interferon γ (IFNγ), a potent inhibitor of proliferation, inducer of apoptosis, and an immune modulator of mammalian cells, has been used as an anticancer agent in cancer therapy. Several molecular mechanisms, depending upon thedifferences in the lineage of transformed cell targets, have been elucidated for the growth inhibition or apoptosis of target cancer cells by IFNγ. However, its mechanism of action on normal cells needs to be understood from the pointof view of: (i) The effect of IFNγ on non-transformed cell line and (ii) The side effect of interferon therapy on normalcells in cancer patients. Using the non-transformed cell line, human foetal epithelial cell line (WISH), our earlier studieshad shown that IFNγ detains cells at a point prior to the activation step of cyclin dependent kinase 2 (CDK2) in the G1 phase of cell cycle. In the present study, we identified significant reduction in the levels and/or activity of cyclin E-CDK2, CDC25A phosphatase, cyclin H, cyclin E, cyclin D, p21 and p27. The drastic decrease in the levels and/or activity ofcyclin E and/or of cyclin E-CDK2 complex might have caused growth arrest of WISH cells by IFNγ.

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87. Bronchial SialadenomaPapilliferum: A Very Rare Cause of Hemoptysis

Purpose: This case is only the third case of the Sialadenomapapilliferum of the bronchial system. This is a extremelyrare tumor of the bronchial system. This report highlights once again the histo-pathological difficulties of diagnosingsuch a rare tumor.

Patients and methods: A 53 year old woman with a 3 weeks history of a productive cough associated with hemoptysispresented to the Community hospital Stuttgart (Teaching Hospital of the University of Tübingen). A thoracic CT revealeda solid mass in the right lower lobe with 10 mm diameter. In the community hospital a bronchoscopic biopsy wassuspicious for an adenocarcinoma of the lung.

Result: The patient was transferred to our institution for thoracic surgery and a right lower bilobectomy withsemicircular intrapericardial vessel resection and total nodal resection was performed. By immune-histochemicalanalysis, the removed tumor (size 10 mm) revealed to be a benign adenoma from the seromucosal bronchial glands,which is a very rare benign tumor of the Sialadenomapapilliferum type. All of the removed lymph nodes were analyzedand showed no signs of malignancy.

Conclusion: At present there have been reported only two cases of the pulmonary Sialadenomapapilliferum in theliterature. This case report represents the first case of pulmonary Sialadenomapapilliferum in Germany and westernEurope. The biologic behavior of this tumor still remains unknown.

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88. Biochemical and Microbial Examination of Sulphi and Cheend: Two Alcoholic Beverages from Central India

Fermented food and beverages have been used worldwide since time immemorial. Various cultures have traditionally been using various fermented products. Beer was brewed by Babylonians and also exported to Egypt around 3000 BC. Borde and tej from Ethopia , boza from Turkey, suusac from Kenya , Fermented milk product from Fulani (a tribe) of Burkina Faso, pulque a traditional Mexican alcoholic beverage, Sobia from Saudi Arabia , BhaatiJaanr from Eastern India, Hamei and Marcha from Sikkim and Manipur are just few fermented food products and beverages. Many others, which are also used, may not have found themselves in the literature. Sulphi and Cheend are such products. Sulphi is extracted from fishtail palm *Caryotaurens* by cutting growing leaf base of the plant and an earthen pot is tied beneath the cut to collect the juice. Similarly Cheend juice is extracted from a palm *Phoenix dactylefera*. Both Sulphi and Cheend are used by the tribal people of Bastar region of Chhattisgarh state of central India. The present work aimed at quantitation of sugar and protein along with bacteria in both these alcoholic beverages.

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