Volume 83 • Supplement
June 2020

ISSN 1726-4901

JCMA

Supplement to

Journal of the Chinese Medical Association

Proceedings of 2020 Congress and Scientific Meeting of the Chinese Medical Association

Chinese Medical Association, Taipei, Taiwan, Republic of China
http://homepage.vghtpe.gov.tw/~jcma/index.htm

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中華醫學會第24屆109年度會員大會

暨聯合學術研討會

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數位醫療2020在臺北榮總

Digital Healthcare 2020 at Taipei Veterans General Hospital

時　間：109年6月6日　　08:30~17:30
Time：June 6, 2020　　08:30~17:30

地　點：臺北榮民總醫院 介壽堂
Place：Jie Shou Hemorial Hall
Taipei Veterans General Hospital

本活動部分經費來自：科技部巨量影像計畫
公益信託林堉璘宏泰教育文化公益基金
財團法人許金德紀念基金會
財團法人沈力揚教授醫學教育獎學紀念基金會
臺北榮民總醫院放射線部

數位醫療2020在臺北榮總
Digital Healthcare 2020 at Taipei Veterans General Hospital

The promotion and future prospect of medical appliance management & unique device identification in Taipei Veterans General Hospital

臺北榮總特材管理 / 單一識別系統之推動與未來展望

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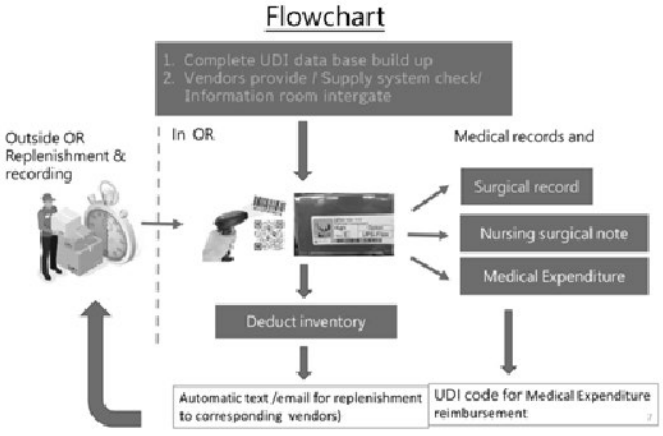
To be a wise hospital, the medical appliance management is crucial to achieve a resource sharing, real-time data, increase efficiency and reduce time and errors of manual input. In addition, electronic medical record with paperless is also an inevitable trend. In order to integrate the management of rapid progression of medical appliance, Taipei Veterans General Hospital start first in 2016 to promote the UDI and independently developed the VGHTPE system with rolling correction as follow:

- Recruit the professional team (Including Deputy Superintendent, Information Room, Supplies Office, Department of Medical Administration, Nursing Department, OR…) and held regular meetings per month.
- "One Object One Code", extend the code from 12 to 15 numbers
- General investigation for the UDI of currently available medical appliance (Grade III medical device first, followed by Grade II & I). Hold an advocacy symposium to announce and enable more vendors to provide the UDI code for their products.
- Flowchart to execute
  - 2017/03 Hardware and software established
  - 2018/2 Initiative in JR for the arthroplasty prosthesis and confirmed the accuracy, 2018/8 Promote to all division in Orthopedics and Surgical department



- Work effectiveness:
  - "One Object One Code" completion rate is 86.94% (5,854 items),completed in Dec, 2020.
  - Over 109,804 electronic automatic replenishment notices send, 686 days manpower saved
- Future Prospect: 1. "One Object One Code, One Price" 2. "Surgical billing and accounts electronization" 3. UDI codes automatic identification

Using big data analysis and evidence-based care strategies to reduce the incidence of falls among inpatients

運用大數據分析與實證照護策略降低住院病人跌倒發生率

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Falls among inpatients are the common accident and serious threat to patient safety. With the aging population, the elderly are at increased risk of falls. Falls-related injuries pose a significant burden to the family, medical and social welfare system. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and Joint Commission of Taiwan (JCT) sets "preventing falls and reducing injury from falls" as the goal of patient safety. Medical institutions are required to establish plans and quality indicators of clinical care to reduce patient falls and evaluate their effectiveness.

The statistics of Taiwan Clinical Performance Index (TCPI) states the average incidence of falls in medical centers from 2011 to 2019 is 0.06%. Nevertheless, the incidence of falls in our hospital had been higher than medical centers until 2018.

It's difficult to prevent all patients from falling accidents in the hospital. However, it's possible to reduce the incidence of falls by using clinical data analysis, practical and evidence-based approaches to fall prevention in the elderly. We analyzing the patient's health status, drug response, environmental or other factors through the fall events in databases. Based on these data analysis, evidence-based information and professional advice form cross-team members, then we develop the recommendations for practice and policy. After analyzing the clinical data, the Nursing Information System (NIS) can intelligently pointed out the high-risk patients of falls to medical team members, and reminding to implement the evidence-based care strategies to prevent falling injury. Moreover, the clinical data are returned to the care units monthly to carry out various qualities improvement interventions. Then we integrate all improvement programs into systematic textbooks, using multiple teaching strategies to promote all units in the hospital and strengthen the cognition and the completeness of practice. In 2019, the incidence of falls is decreased to 0.05% in our hospital, which is better than the average of medical centers.

Early Warning Score vs data-driven model: Predicting clinical compromise in a General Hospital

住院病患之病危預測：比較早期預警系統及資料驅動模型

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Hospital is expected to be the safe place. Early recognition of worsening hospitalized patients is the essential step to prevent deaths. However, intensive assessment by caregivers is costly and not always available in general wards. Early Warning Score (EWS), which was proposed by National Health Service (NHS) of England, is a popular tool for detecting clinical compromises using basic physiological findings. EWS helps clinician to screen out patients who are at risk, but Its efficacy varies and needs to be validated across different institutions. The aim of this study is to retrospectively validate the EWS in predicting death events and compare it to data-driven models in the general wards of our hospital, which has more than 3000 beds

Healthcare data from all hospitalized adult in 2019 were collected. EWS was calculated on an hourly basis. Missing values were handled by forward-filling. Clinical compromise was defined as in-hospital death in the next 24 hours. The EWS was validated by area under the receiver operator characteristic curve (AUROC) and area under the precision-recall curve (AUPRC). We also design a data-driven model using artificial neural network (ANN) and compared its performance to the EWS.

The healthcare data of 110,348 hospitalized adults in our general wards in 2019 was calculated. A total amount of 2,454 death events was identified. The incidence rate of death was 5.3 per 1,000-person-day. 16,189,122 scores were generated. The AUROC and AUPRC of EWS were 0.91 and 0.24 respectively for predicting clinical compromise. Meanwhile, the ANN model achieved AUROC and AUPRC of 0.91 and 0.36 respectively on independent testing dataset.

This study successfully demonstrated the feasibility of EWS in our hospital. Furthermore, data-driven models, which had higher AUPRC, produced fewer false positive signals than EWS, were more suitable for death events prediction in general wards.

Intelligent Pharmacy Practice: The present and future

智慧化藥事作業的現況及未來

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Ensuring the efficacy and safety of patient medication use is the utmost responsibility of pharmacy departments in health care facilities. Medication errors may occur during each step of the medication use process, from the physician prescribing, pharmacist dispensing, to nurse or patient administration. With the advances of science and technology, modern pharmacy practice widely utilizes information techology to ensure the quality of medication use. This session invites the world-class medical center, Taipei Veterans General Hospital, to share their experiences and prospects on intelligent pharmacy practice development. The information systems designed to assist pharmacists during each medication use process will be introduced, including bar-code assisted inventory management system for inventory control; for the prescribing process, 40 automatic error-proofing mechanisms embedded in the CPOE, contraindication checks, and decision supports (e.g. virtual codes for drug duplication checks, auto-dose/frequency conversion for drug shortage substitutions); pharmacists assisting systems such as real-time prescription verification system, inpatient unit-dose dispensing system with bar-code and iPad assistance, traditional medicine dispensing system, drug identification apparatus, drug information kiosk, on-line drug refill reservation system, clinical pharmacist's patient management system, drug information and consultation system, pharmacist anticoagulation clinic service system, CPOE for investigational medicinal products. Ongoing projects such as pediatric dose auto-checks, automated dispensing cabinet (ADC) managing system, drug delivery system, information integration App for case/disease management, perioperative anticoagulation management for pharmacist anticoagulation clinic services, and infrastructure renovations of the new medical building, including smart dispensing counters, ADC for controlled drugs, digitalized medication shelf labeling.

The support from the institution, competent pharmacy staffs, and the collaborations with IT engineers are the three pillars for the development of intelligent pharmacy practice. In the modern ever-changing society, integration of IT, utilization of available resources and constantly re-adjustment of the pharmacy practice are vital to meet the clinical needs.

Promotion, application, development and test of quality of life questionnaires for patients with cancer: Establishing a chemotherapy side effects reporting model incorporating breast cancer patients

癌症病人生活品質問卷推廣應用與研發測試：建立乳癌病人參與協作化學治療副作用填寫模式

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Cancer is the leading cause of death in Taiwan. To improve quality of life (QOL) is of equal importance as to improve survival for patients with cancer. We cooperated with the European Organization for Research and Treatment of Cancers (EORTC) on the translation and development of quality of life questionnaires and updating of existing modules is needed because of newly developed treatments including targeted therapy, immunotherapy, cellular therapy, and minimally invasive surgery. We will aim at promotion and application of questionnaires for breast cancers through collaboration with Taipei Veterans General Hospital by developing user-friendly internet versions. Patients can use these devices at home or during the waiting time to assess their quality of life of different phases of treatment and provide important information with clinical data for their health care and self-health management.

Chemotherapy is one of the most common treatments received by breast cancer patients worldwide. However, side effects of chemotherapy remain under-estimated and neglected, mostly due to high lost of follow up rate and poor compliance from patients undergoing chemotherapy, resulting in a biased estimate of side effects, and patients' subjective quality-of-life perception.

To overcome the limitations, we purpose to establish a novel mobile app to enhance the follow up of breast cancer patients, and a cloud-based database for both physicians and cancer patients. The corroborative database is suitable for physicians to collect clinical data from breast cancer patients and also provides a platform for real-time communication between medical providers and patients to enhance follow up and outcomes assessment.

The mobile app is empowered by a cloud-based corroborative system. The system comprises a data management and storage subunit, a security information subunit, and an instant message communication subunit. Physicians could enter the clinical and treatment data immediately after the completion of chemotherapy prescription with their mobile devices, and sensitive clinical data were secured and restricted to authorized personnel. On the other hand, breast cancer patients could review their clinical and operative details in a well-designed and self-explanatory manner.

We believe the establishment of chemotherapy side effects reporting system, including a mobile app system with a cloud-based dataset could enhance the quality of care for breast cancer patients and facilitate outcomes research for this common disease with a more comprehensive and complete follow up record.

Epidemic prevention in the hospital utilizing information technology

運用資訊科技強化醫院之防疫管理

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為防止 COVID-19 疫情於院區擴散並配合政府政策，臺北榮總建置資訊系統，提供預約、TOCC 登錄、簡訊通知及訪客登記等功能，事先協助病人及陪病、探病民眾進行篩檢，來院時可快速通關，並避免有疫情疑慮之民眾到院，達成防疫之目的。另經由資訊系統作業，減免紙本保存的問題，亦有利於事後查詢及統計分析。

Virtual and augmented reality system increase effectiveness of trainings for occupational safety and advanced OSCE skills

虛擬及擴增實境系統有效培訓年輕醫學生的職安及進階 OSCE 技能

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Medical trainees lack of familiarity and confidence with respect to practicing universal precaution for the prevention of occupational needle stick (NSI)/sharp (SI) injuries may harm themselves. The risk of occupational NSI/SI among junior doctors was 3 times that of senior doctors. Even though most of the trainees report to have received training, the occupational NSI/SI rate remained persistently high. Improper clinical wastes management (CWM) carries a substantial risk to the hospital staff, patients, the community, and public health, as well as the risk of transmission of healthcare-associated infections. Failure to dispose of contaminated needles and syringes in the correct way causes serious threats through dangerous repackaging and recycling. Hence, it is important for well-trained staffs to separate them at the location of they are used. However, a systemic review revealed that healthcare professionals' familiarity and confidence regarding occupational safety including occupational NSI/SI prevention and CWM are not enough. Accordingly, there is considerable room for the training tools and learning flows to be improved. Endotracheal intubation, central venous catheters and difficult clinical communication are advanced OSCE skills that need to be trained among medical trainees. Using virtual and augmented reality (VR-AR) technology in training can improve engagement and increase knowledge retention and satisfaction. In medical education, game-based learning has gained popularity due to an increase in trainees' sustained motivation and engagement. We developed game-based VR-AR training on occupational safety and advanced OSCE skills. The VR-AR system increases the familiarity, confidence and anxiety of new-coming medical trainees. In general, medical trainees and faculties reported that these AR-VR aids meets their needs provided accurate learning messages.

Next generation electronic medical records-intelligent healthcare record in Taipei Veterans General Hospital

新世代的臨床病歷紀錄 - 智慧病歷在北榮

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Medical professionals record patients' symptoms, data, diagnosis, treatment history, and results on medical records. The quality of medical records suggests the quality of the care of medical practice. A reliable and comprehensive medical record can help sound clinical decision on the subsequent treatment strategies and improve patients' outcome. In Taipei Veterans General Hospital, our established a Smart Medical Committee and start developing an intelligent electronic medical record system integrated with clinical reasoning and decision support aid, which is aimed at constructing the embed modules for representative diseases planned by different specialties such as cardiology, surgery, and emergency departments. The establishment of the prototype of the medical record generator can become the basis for the development of intelligent electronic medical records in the hospital. In the initial stage of system introduction, constructing a scientific and innovative learning environment will help not only assist the physicians toward a better medical expertise of medical record writing through the clinical reasoning-integrated system, but also the comprehensiveness and correctness of history taking, clinical thinking, and decision-making skills. The established system may help and promote its clinical uptake in the future and become the foundation of smart healthcare system.

Due to the rapid development of information technologies, smart healthcare has become a more and more important topic. Clinical Decision Support System (CDSS) has been developed for several years and it can assist doctors to improve the quality and accuracy of diagnosis. Recently, artificial intelligence has been widely used in many fields. Particularly medicine with artificial intelligence research has become an important trend. Therefore, we will be focusing on incorporating artificial intelligence techniques into the decision support system to improve the quality of medication. This project is tailored to fit for different kinds of diseases using artificial intelligence techniques, including data mining, machine learning and deep learning methods, so as to construct an effective medical decision support model with incorporations of medication records, literatures and guidelines.

Taiwan Diagnosis Related Groups, Tw-DRGs, is the currently used reimbursement strategy for National Health Insurance. The DRG is determined according to the disease and treatment when a patient is discharged from the hospital. The DRG, length of stay, and other factors strongly impact the operational and financial performance for hospitals. The DRG encoding considers data in various aspects. Factors in the clinical aspect involve of major diagnostic category and major procedure. Other factors related to patients include age, gender, discharge status, and comorbidity or complication. The ICD-10-CM (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Clinical Modification) is a disease classification system adopted by many countries in the world. The novel application of big data has been considered in many hospitals to obtain a consistent encoding result and avoid overlooking diagnosis information. This project aims to establish an ICD encoding system, alone with a DRG logic aligned with the Tw-DRGs. The system will be assisting decision makers to improve efficiencies, simplify their operations and make the right decision on principal diagnosis selection.

Real-time precision medicine: Deep learning-based prediction for cardiovascular risk

即時精準醫學：深度學習模型預測心血管風險

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國立陽明大學 醫學院 醫學系 高齡醫學科

Traditionally, foundations of medical practice were dependent on clinical trials, cohort studies, epidemiological studies and case series. Data collected from these studies were relatively simple and usually using average values for clinical practice. Nevertheless, health state and lifestyle parameters may vary on daily practice and the variation per se has been considered as a health risk. Using real-time and patient-powered data nature from wearable devices, we are able to incorporate time-to-time lifestyle parameters into an artificial intelligence-aided precision health management program. We conducted a prospective cohort study with 319 eligible community-living adults aged 50-85 years with a smart watch collecting lifestyle parameters for 12 months. K-means cluster algorithm divided all participants into three groups, i.e. non-active users (wearing ≤ 2 days), active users (wearing >30 days with at least once both in weekdays and weekend), and usual users (others). LASO, MARS, random forest, SVR and linear regression were compared in model prediction and stability. In this study, multivariable linear regression posed best accuracy and stability. Overall, 128 (40.1%) and 98 (30.7%) were active and usual wearable device users. Multivariable linear regression showed walking speed of active users increased 1.6 m/s (p=0.03) than that of non-active users. Compared to usual users, active users had higher average daily, weekday, and holiday step counts. Walking speed would increase 0.03 m/s when participants had one more thousand daily average step counts (p=0.02). In addition, another study used ECG obtained from smart watch together with other lifestyle parameters to estimate the changes of Framingham Heart Risk Score. Deep learning approach successfully developed a prediction algorithm for the 12-month excessive cardiovascular risk with the accuracy of 70%. To conclude, real-time data with continuous measurements may change the medical practice and facilitate the development of precision health promotion and healthy aging.

Developing and evaluating EHR-driven prediction models for optimizing effective transitional care

建立與導入電子數據為基礎之臨床預測模型優化轉銜照護服務模式

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Patients are extremely vulnerable during the transition from one care settings to another setting. Transitional care gaps often occurred between health care practitioners and settings and led to excessive adverse events and mortalities. Transparent data-driven prediction models would greatly promote continuity of information and clinical management and could be a key to optimize effective transitional care.

In this session, we will share a framework from developing to deploying electronic health record (EHR)-driven prediction model in clinical practice. We had used our electronic health record-database to develop re-admission models for home care patients, which was evaluated by agent-based evaluating framework. The prediction model had greatly aligned care needs and management goals and successfully reduced rehospitalization rates by 40%. EHR-data driven prediction may have a key role in optimizing transitional care.

Untargeted metabolomics predicts the functional outcome of ischemic stroke

代謝體學可以預測缺血性中風功能的恢復

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Metabolites in blood have been found associated with the occurrence of vascular diseases, but its role in the functional recovery of stroke is unclear. The aim of this study is to investigate whether the untargeted metabolomics at the acute stage of ischemic stroke is able to predict functional recovery.

One hundred and fifty patients with acute ischemic stroke were recruited and followed up for 3 months. Fasting blood samples within 7 days of stroke were obtained, liquid chromatography and mass spectrometry were applied to identify outcome-associated metabolites. The patients' clinical characteristics and identified metabolites were included for constructing the outcome prediction model using machine learning approaches.

By using multivariate analysis, 220 differentially expressed metabolites (DEMs) were discovered between patients with favorable outcomes (modified Rankin Scale, mRS $\leq$ 2 at 3 months, n = 77) and unfavorable outcomes (mRS $\geq$ 3 at 3 months, n = 73). After feature selection, 63 DEMs were chosen for constructing the outcome prediction model. The predictive accuracy was below 0.65 when including patients' clinical characteristics, and could reach 0.80 when including patients' clinical characteristics and 63 selected DEMs. The functional enrichment analysis identified platelet activating factor (PAF) as the strongest outcome-associated metabolite, which involved in proinflammatory mediators release, arachidonic acid metabolism, eosinophil degranulation, and production of reactive oxygen species.

Metabolomics is a potential method to explore the blood biomarkers of acute ischemic stroke. The patients with unfavorable outcomes had a lower PAF level compared to those with favorable outcomes.

Integrating pathological images with multi-omics data for breast cancer targets prediction by deep convolutional neural networks: Predicting molecular subtypes of breast cancer

以深度卷積神經網路整合病理影像與多重體學來探勘乳癌治療標的：預測乳癌分子亞型的應用

Nam Nhut Phan[a,b], Chi-Cheng Huang[c], Eric Y Chuang[b,d], Ling-Ming Tseng[c]

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Breast cancer is a heterogeneously complex disease. A number of molecular subtypes with distinct biological features lead to different treatment responses and clinical outcomes. Traditionally, breast cancer is classified into subtypes based on gene expression profiles; these subtypes include luminal A, luminal B, basal-like, and HER2-enriched breast cancer. This molecular taxonomy, however, could only be appraised through transcriptome analyses. Our study applies deep convolutional neural networks and transfer learning from three pre-trained models, namely ResNet50, InceptionV3 and VGG16, separately or in combination for classifying molecular subtypes of breast cancer using TCGA-BRCA dataset for training and Taiwanese breast cancer dataset for validation. Totally 1044 whole slide pathological images from TCGA were used for the training and the validation dataset from Taiwanese population was 60 images. In this study, we attempted to train the model without region of interest labeling from pathologist. The final images labeling were obtained from Genefu package using mRNA expression data. The results showed that our model performance reached to 78% of accuracy for validation. This outcomes suggested that classification of molecular subtypes of breast cancer by pathological images are feasible and could provide reliable results without time consuming from pathologist for images label.

Deep learning in colorectal cancer with lung metastases

結直腸癌肺轉移的深度學習

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Despite the advance in treatment, the median overall survival (OS) is around 30 months in patients with metastatic colorectal cancer (mCRC). Lung is the secondary site of metastasis from mCRC. Grossly, most of patients could not survive mCRC. However, for patients with oligometases, colectomy and metastasecmoy could provide the curative opportunity the 5 year disease free survival was around 23% in patients after colorectal pulmonary metastasectomy. Today, colorectal pulmonary metastasectomy emergy as a new standard in treating mCRC with pulmonary oligometastasis. General speaking, the colorectal pulmonary metastasectomy was advised by chest surgeons if they solitary pulmonary nodule >= 1~2 cm. However, if the size smaller than 1 cm, there was no consistent rule for pulmonary metastasectomy. Most recommendations for pulmonary metastasectomy or not based on extrapolation from lung cancer guideline. To our knowledge, there was not report to discuss rule about pulmonary metastasectomy in patients with small (<10mm) solitary colorectal pulmonary module. For small solitary nodule, it is hard to differentia normal from tumor module. The false positive rate by clinical judgement is aroiund 20-30%. Then patients suffered from unnecessary lung surgery. This difficult in image classification encourage us to use artificial intelligence, machine learning and deep learning in differentiating normal nodule from tumor nodule in patients with colorectal cancer. Our short talk aims to sharing our limited experience in AI models by different program and exploring a model for approaching colorectal solitary small pulmonary nodule in patients' with mCRC.

Automatic Mycobacterium Tuberculosis detection using simple image processing with artificial intelligence(AI)

數位病理：以人工智慧輔助結核病抗酸菌染色檢驗

Wen-Yih Liang
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Microscopic examination of mycobacterial can provide useful information without the prolonged delay time in culture procedures. Pathologist will go through the whole slide in high power field in search of any acid fast stain positive bacterium.

However, this process take many work loading and is time consuming forpathologist despite the result may be controversial. If patient is diagnosed of acid fast stain positive, isolation and preventive medications will prescribe to the people who have ever contact with the patient before. Therefore, it is very important to make an appropriate diagnosis for acid fast stain.

Our research project aim to create a digital analysis method and tool forpathologist to evaluate the acid fast stain slide. We create a convolutional neural network algorithm to pre-diagnose the virtual slide and provide the positive and negative area for pathologist. Besides, if pathologist change the positive or negative output, the changing value will be send back to our training database to improve the algorithm.

As for now, we already build an input program which is compatible with most current image data format (.tif, .bmp, .jpeg, .png, and .gif) and virtual slide format (Aperio, Hamamatsu, Leica, MIRAX, Philips, Ventana, Trestle and Sakura). We split the image into 40 x 40 pixel by small red color object. There is no tuberculosis positive area loss during this process after evaluating our current 20 positive slide. Annotation will be done by pathologist and the result will be built into Google TensorFlow using mini-batch stochastic gradient descent algorithm to training our convolutional neural network.

Infant's general movement assessment by AI-assisted Pose-Estimation for early detection of children's neurological deficit

運用人工智慧輔助判讀嬰兒整體運動以協助早期偵測幼兒神經發展異常

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With the advancement of neonatal care, there is an increase in survival rate and decrease in complications in high-risk neonates. However, a few sick infants may survive with neurological sequelae. Infant's general movement assessment (GMA) evaluation is known to have good predictions on future neurological deficits, such as cerebral palsy or severe mental retardation. In contrast to regular neurological examination, GMA relies on professional observation of infants' spontaneous movement, which is time- and labor- consuming and thus limits its universal application. In this study, we applied artificial intelligence (AI)-assisted pose-estimation algorithms to facilitates GMA by automatically analyzing videos record from infants and demonstrates its validity.

Infants younger than 5 months old were enrolled, and corrected age were applied on preterm infants. Cameras were set at the 50 cm height above infant's incubator or bed to record their spontaneous movements for 10-15 minutes. The video records were evaluated by 2 experienced physiotherapists for professional GMAs. Also, these videos were transformed to be 25 images/sec with size of 1920x1440 pixel by computer technicians. Then, each image was marked for the movement of 4 limbs, including 15 joints (head, neck, buttock, and bilateral shoulders, elbows, wrists, hips, knees, and ankles). The joints' angles were calculated, and transformed with time schedules. These images were first feed into a pre-trained public pose-estimation model, which generates "key points" as representation of major joints of infants. We adjusted preliminary predictions and use them to retrain the original model for better fitting of infants' scenario. The correspondences of key points signals generated from the model and result judged by expertise were analyzed.

A total of 70 infants finished the video recording and professional GMAs from August 2019 to April 2020, including 49 full-term and 21 preterm infants. The results of professional GMA readings were 38 normal, 8 abnormal, and 24 uncertain findings. In 6 preterm infants with abnormal GMAs, all of them were extremely-low-birth weight infants (birth weight < 1000g). In 2 full-term infants with abnormal GMAs, one infant had congenital anomaly and craniosynostosis, but other one had no disease history. Our AI-assisted pose-estimation model for the recorded videos had high positive detective rate in both enrolled preterm and full-term infants. Further evaluation and follow up their long-term neurodevelopment are important to confirm its prediction accuracy.

In conclusion, we developed an algorithm to facilitate GMA using AI-assisted pose-estimation, which made GMA more feasible in clinical scenario. Hopefully, this system may be able to increase diagnostic rate in high-risk infants and compensate the lack of professionalisms in this field.

Use of Artificial Intelligence in assistance of colonoscopy

利用人工智慧輔助大腸鏡檢查

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Colonoscopy has been widely used in clinical practice since Drs. Shinya and Wolff first applied fiberoptic endoscopy to examine the entire colon 50 years ago. Currently, colonoscopy is extensively conducted worldwide for the optical and histologic diagnosis of suspected colon lesions, resection of adenomatous polyps, hemostasis of bleeding, dilation of luminal strictures. The wide application of colonoscopy in the surveillance program to prevent colorectal cancer further increases the colonoscopy volume required. In recent years, artificial intelligence (AI) has been increasingly used in endoscopy. Application of the concept and technology of computer-aided diagnosis (CAD) for colonoscopy has also been tried in polyp detection, polyp characterization inflammatory bowel disease grading and cecal intubation identification. With AI assistance, the quality of colonoscopy may increase. We used convolutional neural network (CNN)-based algorithm to analyze the colonoscopy images and videos in our endoscopy center to build up several algorithms to assist colonoscopy in detection of lesion, identification of lesion and colon preparation quality evaluation. Further prospective clinical studies in evaluating the efficacy of AI algorithm in assisting colonoscopy practice and training are warranted in the future.

Brain atlas for psychiatric disorders and smart brain imaging assessment platform

精神疾病大腦圖譜與智慧腦影像評估平台

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Brain atlas is an important reference tool for studying brain function. At present, brain atlases define brain regions based on histology of neurons or anatomical structures, but there has not been any research on brain atlases specifically related to mental disorders. In recent years, psychiatric diseases have made great progress in both drug treatment and etiological research. However, the diagnosis of mental illness still relies on descriptive criteria and lacks objective diagnostic markers. Among many brain-related biomarkers, neuroimaging is the most important tool for studying brain. The recent rise of medical big data and computer sciences has led to the rapid development of artificial intelligence in medical applications. Artificial intelligence algorithms may be able to help find inconspicuous changes in brain images, combined with statistical information as important information to establish the brain mapping of psychiatric disorders. Therefore, our team aims to use the big data of magnetic resonance imaging to establishing brain mapping of schizophrenia, bipolar disorder, and unipolar depression. We have documented brain mapping of psychiatric disorders at different levels through structural, functional, diffusion tensor imaging, and genome-wide big data. This atlas will be able to provide relevant brain structures or dysfunctional brain regions for objectively differentiating mental illnesses. We have also integrated the research results of the brain mapping of mental illness and build a web-based platform for the visualization purpose. We anticipate that the platform may provide advanced information regarding the brain pathology of psychiatric diseases, characterizing by individualized diagnosis and clinical explainability.

Evolutionary learning for prediction of recurrence time using computed tomography images and clinical data on liver cancer

演化學習使用電腦斷層影像和臨床數據預測肝癌復發時間

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Prediction of recurrence time and overall survival time plays an important role in the treatment strategy of patients with liver cancer. Recently, the studies on the analysis and prediction of high-risk factors in diseasing recurrence focused on macroscopic vascular invasion and liver functions.

This study proposes an evolutionary learning method to predict the recurrence time after therapeutic surgery using clinical data of 31 features and computed tomography (CT) images on liver tumor with annotation. The extraction of candidate features from the annotated liver tumor on CT images mainly includes texture, moment, morphology, edge and intensity features. The feature selection for both image and clinical features and parameter setting of support vector machine are simultaneously optimized using an inheritable bi-objective combinatorial genetic algorithm to identify a small set of informative features while maximizing the prediction accuracy.

There are 517 patients who were followed more than one year. The ratio of the training and test samples after therapeutic surgery was about 7:3. The prediction accuracies of one-year recurrence using 10-fold cross-validation and independent test were 77.46% and 72.73% using 26 clinical features on average, better than some compared methods. The proposed evolutionary learning approach can also be used for predicting the overall survival time after transarterial chemoembolization in the hepatocellular carcinoma patients. There are 204 patients with overall survival time and 46 clinical features without missing values. The proposed method achieved a correlation coefficient of 0.76 using 10-fold cross-validation.

The analysis on the identified clinical features supports the proposed prediction methods. The prediction model provides valuable information for decision making of personalized treatment strategy.

High performing and efficient diagnostics using federated, privacy preserving AI

利用具隱私保護的聯合學習技術，訓練高效能的輔助診斷人工智慧

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Brain tumor diagnostics using magnetic resonance imaging (MRI) scans is a time consuming and laborious task even for the most experienced doctor. By leveraging computers and intelligent software it is possible to perform this task completely autonomously, thus freeing up time for the medical professionals to spend on other tasks. One such promising technique is to use deep learning and artificial intelligence (AI). However, this comes with several challenges in terms of patient privacy. The question then becomes how do we enable the strength of big data without harming the integrity of our patients? The answer to this question is to leverage a novel idea called Federated Learning, which is the topic of this talk. It will be shown that Federated Learning can be used to make our AI models significantly more accurate by cooperating between an arbitrary number of hospitals – without leaking any sensitive information. AI is all about having access to large amounts of data, amounts that are much larger than any single hospital can have on their own but pooled together across institutions it is indeed doable. In the talk I will present preliminary results from my study that illuminates the enormous potential of said technique. It will be shown that a model that is trained across institutions performs significantly better than if each hospital attempts to build their own models. The future of AI assisted healthcare spells collaboration.

Utilization of Influential Scores to improve the explainability of deep learning models

運用影響指數於深度學習模型以提昇可解釋性

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Deep learning has been widely adopted in a variety of fields, such as medical treatment, medical images, and AI. It can help to provide the neural network model for prediction, but it is difficult to explain the important features. On the other hand, the technique of I-Score can extract important features from a large number of variables. Hence, it can enhance the explanability of the prediction model. In the CAM graph of deep learning, we propose to explore important features predicting the target by the technique of I-Score. Consequently, we integrate the methods of deep learning and I-Score to discover important features that can improve the explainability of prediction model in this study.

Segmentation of vestibular schwannoma from multi-parametric MR images using dual-pathway U-Net model before and after gamma knife treatment

利用深度學習自動分割加碼刀治療前後聽神經瘤病灶

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Manual delineation of vestibular schwannoma (VS) from magnetic resonance (MR) imaging is required for Gamma Knife radiosurgery (GKRS) and follow-up tumor volume measurement. We retrospectively collected multi-parametric MR images before and after the radiosurgery (GKRS) treatment. The tumor contours were delineated manually by experienced neuroradiologists. However, only the information of tumor contours before GKRS treatment were reserved in the retrospective data. In this study, we aim to automatically segment the VS not only from pre-GKRS multi-parametric MR images but also from the pre-GKRS images in which the tumor volumes without contour information were provided.

We proposed a dual-pathway U-Net architecture using two sizes of convolution kernel to respectively extract the in- and through-plane features of anisotropic MR images. An effective and automatic preprocessing pipeline was also implemented. Multiparametric MR images, namely, T1W with contrast (T1W+C) and T2-weighted (T2W), from 516 pre-GKRS VS patients were used as the training input to build a Convolutional Neural Network (CNN) for segmenting tumors with solid as well as cystic parts.

This pre-GKRS model was used to predict each subject's follow-up VS tumors contour after GKRS. Twenty-one predicted follow-up contours were confirmed or revised by experienced neuroradiologists and further used as new training data for model refinement. Our results demonstrated that (1) the dual-pathway model trained by two-parametric (T1W+C and T2W) images achieved dice scores 0.88 ± 0.06 on pre-GKRS data; (2) the relative absolute volume difference (RAVD) computed from the clinically estimated tumor volume and the predicted follow-up tumor volume using the pre-GKRS model achieved 0.11± 0.06; (3) the RAVD of the clinically estimated tumor volume versus predicted follow-up tumor volume obtained from the refined model improved to 0.1± 0.06.

Device-agnostic AI model for brain metastasis: Deep active learning over a nationwide population-based medical image database

以全國人口醫學影像資料集再精進人工智慧診斷模型

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Imaging variations of magnetic resonance imaging (MRI) from different vendors and protocols could restrict full-fledged usage of an AI model. We leverage a nationwide medical database and aim to alleviate the concern and enable the resulting AI system to achieve inter-device as well as inter-hospital generalizations.

A segmentation model (DeepMets®) for brain metastasis is initially trained on a homogeneous labeled MRI dataset at Taipei Veterans General Hospital (VGHTPE), reaching 87.68% DSC (dice similarity coefficient) in the in-house test set. To improve generalization across various MRI settings, we iteratively refine the model by employing active learning over a nationwide population-based medical imaging database (collected from Feb. 2018-June 2019) at the National Health Insurance Administration (NHIA), Taiwan. With similar enrollment criteria as of the initial dataset at VGHTPE, 3153 patients are filtered out from 3,174,155 MRI series of the database. In each active learning cycle, 200 data points with the highest entropy values are manually annotated and added to the labeled training set. We evaluate our approach using the 2.5D ResNext101 U-Net architecture with Squeeze-and-Excitation block and self-attention mechanism. The network is trained on a combination of multiclass binary cross-entropy and DSC loss. Furthermore, a test set with 120 patient-examinations is formed and categorized according to MRI vendors (three major manufactures on the global market) as well as different diagnostic difficulties. Both initial (DeepMets®) and refined models (DeepMets-Plus) are evaluated on the test set to demonstrate the robustness.

DeepMets® suffers from severe performance degradation, 48.55% DSC (Precision: 45.11%, Recall: 78.67%), in the test set. After refining the model with the nationwide medical database at NHIA for three active learning cycles, its best performance yields 83.84% DSC (Precision: 88.97%, Recall: 87.99%). The results are also shown to be coherent across MRI from different vendors except for the difficult cases.

We demonstrate the development of a device-agnostic artificial intelligence (AI) model for brain metastasis segmentation by exploring a nationwide medical database. The model achieves great generalization on MRI of various vendors and settings across the country and is applicable globally. It is one of the ways to increase model generalization across MRI vendors and settings in addition to federated learning.

Part of material was submitted to RSNA-2020.

Acknowledgement: The study has been supported in part by grant MOST106-2634-075-001- (2018-2020) and National Health Insurance Data AI Application Pilot Project (全民健康保險資料人工智慧應用試辦計畫)

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大腸直腸癌的精準化治療

Precision Treatment for Colorectal Cancer

主辦單位：中華醫學會
協辦單位：中華民國大腸直腸外科醫學會
社團法人中華民國大腸直腸癌關懷協會

時　間：109年6月6日　08:20~17:30
Time：June 6, 2020　08:20~17:30

地　點：臺北榮民總醫院 致德樓第一會議室
Place：The First Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

大腸直腸癌的精準化治療
Precision Treatment for Colorectal Cancer

Welcome to the era of precision and preservation in rectal cancer surgery

直腸癌手術在精準醫學時代的角色

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Main goals of rectal cancer treatment have been and will always be oncological safety and organ function preservation. Over the past two decades, neoadjuvant chemoradiation therapeutics have played key roles in the advancement of retal cancer treatment – particularly in achieving decreased local recurrentes rates and increased spincter preservation rates. Unfortunately, patients who receive neoadjuvant therapy frequently experience associated toxicities years later. As a result, recent data has strongly pushed for the redesign of neoadjuvant treatments. Areas of priority include radiotherapy order and frequency, chemotherapy agent choice and interval of administration, and surgical intervention timing and necessity.

On the other hand, effective primary tumor surgical resection remains an essential component in treatment of both early and advanced rectal cancer. Advancements in surgical instruments and approaches have synergistically driven the evolution of surgical intervention in general. Minimal invasiveness, increased functional preservation, and decreased treatment-related complications have thus emerged as areas of emphatic focus.

In this presentation, we will present data from our own institution and analyze findings from recent publications in order to propose new fundamentals and future directions for the treatment of rectal cancer.

How to overcome challenging colorectal ESD

如何克服具有挑戰性的大腸直腸內視鏡黏膜下剝離術

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Endoscopic submucosal dissection (ESD) is an effective treatment for early-stage gastric and colorectal neoplasms. It enables en bloc resection with tumor-free margins and is not limited by lesion size or location. ESD also offers detailed histological evaluation of surgical specimen and accurate diagnosis of resection margins. Meta-analyses disclosed that ESD is much more effective than endoscopic mucosal resection (EMR) in terms of en bloc resection, complete resection, curative resection, and local recurrence. Although ESD tends to result in better clinical outcomes than EMR, it requires a high degree of training and technical skill. ESD is technically difficult because of the thin wall and various structure of the gastrointestinal tract. For inexperienced endoscopists ESD carries a higher risk of complications such as bleeding, perforation, and longer procedure times as compared with EMR. Fibrosis beneath a lesion makes ESD much more difficult to perform. Several previous studies have reported that fibrosis increases the risks for incomplete tumor resection and perforation. The scar is associated with submucosal fibrosis and is also the most important preoperative predictor of ESD difficulty. During submucosal dissection, maintaining visualization and stable positioning of the endoscope in the cutting area is important and requires a high level of skill. Forming the mucosal flap after beginning submucosal dissection is the most critical part of the procedure. If the mucosal flap can be lifted with an attachment fitted to the endoscope, creation of the mucosal flap improves visibility in the cutting area and allows for easier and accurate dissection. Several strategies have been reported for ESD with severe fibrosis. The use of ancillary devices might enable dissection of severe fibrosis. The development of devices or methods to overcome difficult dissection of fibrosis is necessary.

Techniques to make laparoscopic right colectomy with D**3** lymph node dissection more perfect

腹腔鏡右側結腸切除術的精確淋巴結廓清術

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Recently, there are many evidence that D3 lymph node dissection (LND) shows improved survival outcomes than D1 or D2 LND in right colectomy for colon cancer. And laparoscopic surgery for colon cancer has better short-term outcome than open surgery. Therefore we have to able to laparoscopic right colectomy with D3 LND.

D3 lymph node dissection in laparoscopic right colectomy is a technically challenging procedure. Although the colorectal surgeon has excellent surgical skills and abundant anatomical knowledge, considerable experience is needed to overcome the learning curve. So, in this lecture, I introduce the technique to overcome the learning curve easily and to make the procedures more delicate and faster.

Perineal stapled resection with linear staplers for external rectal prolapse

經由會陰部使用線狀切除器治療外部直腸脫垂

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Rectal prolapse is classified into external prolapse and internal prolapse. Rectal prolapse is an anatomic abnormality and requires surgical resection. Numerous procedures have been described for the treatment of complete rectal prolapse, and these are classified as perineal or abdominal approaches. Perineal procedures such as the Delorme procedure, Altemeier operation (perineal rectosigmoidectomy), Thiersch procedure (anal encirclement), McCann procedure, Lockhart-Mummery operation, and Wyatt perineal rectopexy are suitable for older and high-risk patients. The Delorme and Altemeier procedures are the most commonly used perineal procedures. Recently, internal rectal prolapse has been successfully treated with stapled transanal rectal resection (STARR) using circular staplers. Then, Roland et al. modified the STARR procedure to resect external rectal prolapse. Tepetes described a local treatment for loop colostomy prolapse using a linear stapling device. Now, we have modified this technique to treat external rectal prolapse using 2 linear staplers.

Intraoperative use of ICG fluorescence during colorectal surgery

結直腸外科手術中 ICG 螢光顯影的應用

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Background: Anastomosis after colorectal resection is crucial. Because leakage of anastomosis will cause severe morbidity even mortality. The important factors to secure anastomosis including tension free technique, sufficient blood supply to provide oxygen and nutrient. We judge these factors by personal experience, including perfection of anastomosis. This study tried to evaluate the usefulness of intraoperative assessment of anastomotic perfusion in laparoscopic colorectal surgery by using indocyanine green (ICG) enhanced fluorescence.

Methods: Between July 2018 and January 2019, all resection margins and anastomosis in laparoscopic colorectal surgery were investigated by using fluorescence angiography intraoperatively to assess colonic perfusion prior and after completion of anastomosis. The clinical results were fallow up also.

Results: During this period, a total of 35 laparoscopic colorectal surgery were enrolled, including 4 right hemicolectomies, 7 left hemicolectomies, 11 anterior resections (AR), 3 low anterior resections (LAR), 9 total mesorectum excision (TME) and 1 segmental resection. The surgical team judge the distal part blood flow of the proximal bowel sufficient or not. Then re-judge again after fluorescence performed. There were 2 cases changed the resection margin. One post-OP anastomotic leak due to poor interpretation. No other leak including TME cases.

Conclusion: ICG-enhanced fluorescent angiography provides useful intraoperative information about the vascular perfusion during colorectal surgery. It may lead to change the site of resection, anastomosis, and further, the need of stoma for low lying anastomosis. Another advantage is easier to explain to patient's family about the surgical outcome by showing photo to them. Large RCT is needed to provide evidence of benefit for its routine use in colorectal surgery.

Precision radiotherapy for oligometastases from colorectal cancer

結腸直腸癌患者寡轉移病灶的精準放射治療

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Colorectal cancer is an important disease worldwide. Surgical resection of oligometastases from colorectal cancer (CRC) origin is a widely accepted option for many patients. The majority of the resections are for liver and lung metastases. For those who are medically inoperable or decline surgery, extracranial stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) has emerged as another treatment option. In contrast to conventional radiotherapy, SBRT was delivered with higher radiation dose per fraction (usually greater than 6 Gy) in fewer fraction number (usually less than 5) to a relatively small tumor volume. The randomized SABR-COMET trial showed SABR could procure better overall survival in patients with oligometastatic cancers when compared with those receiving standard palliative care treatments alone. Because liver and lung are movable organs, special technique such as image guidance is used to deposit high-dose radiation precisely. Since 2012, we installed an image-guided intensity modulated radiotherapy (IG-IMRT) machine or Tomotherapy in our department. For liver metastases, I gave 35 to 45 Gy in 5 fractions with Tomotherapy to 12 patients with primary colorectal cancer. For lung metastases, 24 to 45 Gy in one to 5 fractions was conveyed to 3 patients with the same technique. Toxicities were mild. Tumor response will be shown in this presentation. In the near future, carbon ion radiotherapy (CIRT) can also be applied precisely to patients with liver and lung metastases in our hospital.

Evolution of precision medicine: From science to value in colorectal cancer

大腸直腸癌精準醫療之演進：從科學到臨床

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Precision medicine is poised to have an impact on metastasis cancer patients. As the development of genome-based technologies has accelerated, the trend of cancer treatment has changed from chemotherapy to targeted therapy and immunotherapy. In 2019 *Nature Medicine*, 3 important publications, I-PREDICT, TARGET, and WINTER showed us how next generation sequencing (NGS) can help clinicians find an effective treatment for individual cancer patients.

The NGS-based comprehensive genomic profiling (CGP) can detect a wide range of genetic alternations, which increases opportunities to find actionable targets for cancer patients. A good example is the NTRK fusion, which is a rare genomic alteration found in a wide variety of adult and childhood tumor types, and all can respond well to TRK inhibitors. Also, through CGP, the information of microsatellite instability-high (MSI-H) and tumor mutational burden (TMB) are also available to guide the decision of using immunotherapy.

CGP is still not yet widely used in Taiwan due to no public reimbursement; however, its benefit is evident. I will briefly introduce the clinical utility of CGP and the current clinical evidence in CRC, as well as my personal experience in the real-world setting using CGP to guide cancer treatment.

Role of molecular pathology in precision medicine for colorectal cancer

分子病理在大腸直腸癌精準醫療的應用

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Since the introduction of targeted therapies in colorectal cancer, there has been an increased application of the molecular stratification for personalizing treatment. The goal is to define and identify meaningful subgroups and to apply tailored approaches for patient management. The use of biomarkers in personalizing treatment for patients with metastatic colorectal cancer have already begun to transform clinical practice. For example, it is now standard of care that all candidates for anti-EGFR therapy undergo expanded RAS mutational analysis, including KRAS and NRAS genes, to identify RAS mutated patients. Activating mutations in these genes lead to constitutive activation of the EGFR–MAPK signaling pathway and resistance to anti-EGFR monoclonal antibody therapy. In addition to RAS mutation, the presence of BRAF V600E mutation also appears to predict reduced benefit from anti-EGFR therapy. Moreover, BRAF V600E mutations also has been recognized to confer poor prognosis in colorectal cancer.

Microsatellite instability (MSI) or mismatch repair (MMR) is another important biomarker in the management for colorectal cancer patients. Testing these biomarkers allows patients with mismatch repair-deficient (dMMR) tumors and Lynch syndrome to be identified, leading to proper disease risk stratification and optimal therapy for these patients. Moreover, high microsatellite instability (MSI-H) has been recognized to be a favorable prognostic marker in colorectal cancer, but also predicts for a lack of benefit from 5-FU chemotherapy in the adjuvant setting. Recently, MSI-H or dMMR has shown importance in the metastatic setting because of its role as a tissue-agnostic biomarker for immunotherapy.

For RAS/BRAF wild-type colorectal cancer, a growing array of potential therapeutic targets in other oncogenic pathways are being identified. For example, cancers with HER2 amplification may benefit from anti-HER2 therapies. Somatic oncogenic fusions in the NTRK genes are rare in colorectal cancer (<1%), but can confer marked susceptibility to TRK inhibitors. Increased integration of these novel biomarkers is expected in the clinical practice, and will further improve outcomes for patients.

Precision medicine in the real world: Experience from VGHTPE

精準醫療在真實世界的應用：臺北榮總的經驗

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Over the last decade, there have been significant advances in the molecular characterization of colorectal cancer. Up to our knowledge, colorectal cancer is a heterogeneous cancer and it could be classed into several subgroups by location, RAS, BRAF, MSI as well as NTRK..etc. Despite the advanced in treating metastatic colorectal cancer, the median overall survival was around 30-36 months. Even in the era of immunotherapy, only the MSI-H colorectal cancer (2-4%) is response to immunotherapy with anti-PD-L1 and anti-PD1 agents.

The next-generation sequencing technologies (NGS) is now widely used in approaching colorectal cancer treatment. The market for NGS has grown dramatically since the technology was first commercialized, but the main conflicts in NGS for diagnostics is encountered between the “result of NGS” and the “drug choice”.

Our short talk examines the latest advance in treating metastatic colorectal cancer, discussing not only on the treatment strategy, but also clinical application of NGS in treating colorectal cancer as well as the tool for understanding the gene-based knowledge. Also, we would like to report several patient with NGS data in VGHTPE and our limited experience in NTRK detection.

Modification of treatment plan by molecular markers in advanced colorectal cancer

分子標記對晚期大腸癌治療模式的應用

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臺北榮民總醫院 外科部 大腸直腸外科 及 國立陽明大學 醫學院 醫學系 外科學科

Despite advances in screening and therapeutics, cancer continues to be major cause of death worldwide. Currently, for assessing initial tumor bulk or for defining treatment response in solid tumors, physicians will introduce image-based Response Evaluation Criteria in Solid Tumors (RECIST) as the gold standard. However inconsistence between inter- and intraobserver and crude categorization limit the use of RECIST. Blood biomarkers, for example CEA, at present use could improve use of imaging-based assessment, but the sensitivity and specificity are moderate. As the molecular technique progresses, detection of cell-free tumor DNA (ctDNA) in blood has become clinical feasible.

In advanced colorectal cancer, the standard treatment is surgery and adjuvant chemotherapy(FOLFOX). Even with 6-8% improvement of survival, patients will suffer from a lot chemotherapy induced toxicities. Recent studie provided evidences that low risk patients could get similar benefits with shorter course of oxaliplatin-base chemotherapy. ctDNA level after operation could be a surrogate marker of minimal residual disease and as the guide how to determine the duration of chemotherapy.

In metastatic disease, ctDNA level and mutations could be used as choice of the target therapy selection. Also, ctDNA could be the marker of disease status in mCRC patients.

In addition, the consensus is needed to deal with the issue about inconsistence of techniques and lack of reference marker in detection of ctDNA. Besides this, the ability to detect tumor DNA mutations in a blood sample (i.e., a liquid biopsy) would allow an easy to obtain, noninvasive, and quantifiable method for use in the clinical setting to identify candidates for specific therapies and monitoring of disease status over time. It would also provide real-time assessment of mutational status without having to rely on archival specimens from the original primary tumor (if available) or the need for invasive biopsy procedures of a metastatic site.

Optimization of mCRC treatment: The best sequencing in ***RAS***-wild type mCRC

優化轉移性大腸直腸癌的治療：對於野生型 RAS 的轉移性大腸直腸癌最佳的治療策略

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陳國興

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With the advance of chemotherapy, targeted therapy and immunotherapy in the recent 20 years, the median survival of metastatic colorectal cancer (mCRC) patients is largely prolonged. On the other hand, how to choose frontline therapies to achieve the best outcome becomes more complicated. Biomarkers, such as expanded *RAS* and *BRAF* mutations, have been documented to predict the efficacy of anti-EGFR and anti-VEGF monoclonal antibodies. The lack of efficacy of anti-EGFR antibody in *RAS* mutant mCRC has been shown in many randomized clinical trials and thus anti-VEGF antibody is the only recommended targeted therapy in first line therapy. In *RAS* wild type mCRC, both anti-EGFR and anti-EVGF antibodies have clinical benefits with combination of chemotherapies. Thus, primary tumor site may be needed to guide us to choose which type of antibody is the favored one. In this section, I will review the current evidence about comparison of the efficacy of anti-EGFR and anti-VEGF antibodies in frontline therapy for mCRC. I will also discuss about the clinical implication of early tumor shrinkage and deep response. In summary, for left-sided *RAS* wild type mCRC, current evidence support better survival in anti-EGFR treated groups. For right-sided *RAS* wild type mCRC, the survival data is controversial but the response rate may be similar between anti-EGFR and anti-VEGF treated groups. Finally, the differences of two anti-EGFR antibodies will also been reviewed and presented.

Clinical advance in HIV screening and treatment

愛滋篩檢與臨床治療之進展

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After HIV epidemics since 1984 in Taiwan, the number of newly diagnosed HIV-infected were found to be decreased in the past 10 years. The tremendous achievement is considered to be associated in many aspects of HIV diagnosis and treatment. The global action is to increased diagnosis rate, let newly diagnosed patient to receive combination antiretroviral therapy (cART) as soon as possible, retained in HIV care, and maintain high viral suppressed rate. Therefore, treat as prevention is the core strategy to prevent HIV infection. In addition, treatment options for patients with HIV-1 infection have grown over the past two decades to include multiple fixed-dose combination pharmacotherapies that have greatly simplified administration of antiretroviral therapy (ART) for both patients and providers. Effective virologic control can often be achieved with once-daily use of a single-tablet regimen. Over the past three years, ART drug development has focused on the next generation of fixed-dose combinations for initial and maintenance therapy with improved efficacy, safety and tolerability. However, the traditional dogma of effective ART containing at least three active antiretroviral drugs is being challenged by promising data to support efficacy of certain regimens containing two drugs. Moreover, preliminary data regarding long-acting agents combination also provided promising results although more trial results are needed. The antiretroviral therapy is moving forward for the next decade. All these improvement can help us for better HIV control in the future.

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高階心臟影像論壇

Cardiovascular Image Summit

協辦單位：中華民國心臟學會

時　間：109年6月6日　　08:30~16:30

Time：June 6, 2020　　08:30~16:30

地　點：臺北榮民總醫院 致德樓第二會議室

Place：The Second Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

高階心臟影像論壇
Cardiovascular Image Summit

Application of CT imaging in atrial arrhythmias

電腦斷層影像於心房心律不整之應用

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Atrial fibrillation (AF) represents a significant clinical care burden and is associated with substantial risk of stroke and cardiovascular mortality. The genesis of AF is in close relationship to the arrhythmogenic substrate of atria. Therefore, a comprehensive assessment of atrial anatomy, cardiac chamber size and function is essential for better understanding the pathophysiology of atrial arrhythmias. Since catheter ablation for pulmonary veins and left atrium becomes more popular to achieve the curative treatment of AF, cardiac imaging plays a vital role in term of selecting the appropriate candidate, improving treatment outcome, avoiding ablation complication, and post-ablation follow-up. Recently, innovations in advanced imaging with cardiac computed tomography (CCT) promote the ability to delineate the functional remodeling of cardiac chamber, exclude thrombus and guide left atrial appendage (LAA) closure or catheter ablation of AF. This presentation will illustrate the application of cardiac CT imaging in the precise evaluation of the size and function of atria, pulmonary vein and LAA, discuss clinical implication of epicardial fat and highlight importance of CCT techniques to guide catheter ablation of AF and LAA occlusion.

Imaging application in congenital heart disease with arrhythmia

先天性心臟病心律不整的影像應用

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台大兒童醫院 小兒部

With the advance of surgical technique and perioperative care, the long term survival improved significantly in congenital heart disease patients, and the long term complication including arrhythmia became an important. The prevalence of arrhythmia in these CHD patients increased with advanced age and may occur in up to 40 % in complex CHD patients. Arrhythmia has great impact on morbidity and mortality, and catheter ablation has become the mainstay treatment modality. However, ablation outcome is poorer in the CHD compared to other acquired heart disease, because of complex anatomy and arrhythmia mechanism. Image study has become an important part to guide the arrhythmia ablation and improve outcome.

Many new imaging modalities including CT image, Cardiac MRI, intracardiac echocardiography, and integrated fluoroscope can now be applied to the electromagnetic mapping system and assist catheter ablation. First, it is often used before procedure to know the hemodynamic and structural evaluation. Second, use the fusion imaging, we can clearly know the actual geometry of the complex cardiac morphology. Third, it can be used as intra-procedural assessment using real-time intracardiac echocardiographic monitoring. We can use it for vascular access guidance, catheter navigation monitoring, and early detection for potential complication. Most importantly, the use of this imaging can greatly reduce fluoroscope use, and zero-fluoroscope ablation for complex arrhythmia in complex CHD is now feasible.

New insights in CMR imaging of hypertrophic cardiomyopathy

肥厚型心肌病變核磁共振影像新觀點

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Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiomyopathy and is inherited in the autosomal dominant pattern. Cardiovascular magnetic resonance (CMR) has been used for phenotypic description of variants of HCM and late gadolinium enhancement has been used to risk stratify patients for sudden cardiac death and heart failure. Additional imaging features such as abnormalities with mitral valve apparatus, papillary muscles, and spiral pattern of hypertrophy will be presented. We will discuss the phenotypic and genotypic relationships, the utility of newer CMR non-contrast-based tissue characterizations such as T1 mapping and T1rho mapping, and the value of strain in HCM. We will discuss how to use different CMR techniques to differentiate HCM from many hypertrophic mimics such as cardiac amyloidosis, hypertension, LV non-compaction, Fabry's, Danon disease, and athlete's heart. Advanced image analysis such as fractal analysis and radiomic analysis will contribute to risk stratification in the future.

The arrhythmogenic substrate and catheter ablation of ventricular tachycardia in the patients with cardiac sarcoidosis

正子攝影、電腦斷層及核磁共振影像於發炎性心肌病變之應用

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Cardiac sarcoidosis (CS) has a potential risk of ventricular tachycardia (VT) and sudden death. The active inflammation and subsequent myocardial fibrosis were the main cause of disease. The arrhythmogenic substrate of VT in patients with CS has been reported to be myocardiac scar, resulting in development of scar-related reentrant VT.

The disease activity was detected by 67Ga-scintigraphy or FDG-PET as inflammation of cardiac tissue. On the other hand, the late gadolimium enchantment (LGE) of cardiac MRI related to cardiac fibrosis and related to increase arrhythmic events. Both modalities should be important to decide the ablation strategy before ablation. However, there was no date indicating which is most predominant cause of VT in this disease, inflammation or fibrosis.

Catheter ablation was undergone in 22 patients (10 males and aged 62±9) with CS and monomorphic VT. Mean LVEF was 37±18%. The corticoid steroid was administrated in 16 patients (72%) before ablation. The QRS morphology of clinical VT showed LBBB in 11 (50%) and 11 (50%) in RBBB. Epicardial approach was required in 4 of 22 patients (18%). The clinical VT was suppressed after ablation in 12 patients (57%) and 10 patients (83%) had no recurrence during 43±53 months follow-up.

The origin of VT defined by the activation map during VT or pace map was consistent with the site of LGE in 82% and the site of positive 67Ga-scintigraphy or FDG-PET in 35% ($P < 0.05\%$)

Conclusion: The tissue fibrosis was a predominant arrhythmogenic substrate in the CS.

The role of echocardiography in cardiomyopathies

心臟超音波於心肌病變的角色

Luigi P. Badano, Honorary FASE, Honorary FEACVI

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Echocardiography plays an important role in the initial evaluation, diagnosis and management of patients suspected of having a cardiomyopathy. In patients with suspected cardiomyopathy, echocardiography is the most common initial imaging test used to establish the presence of cardiomyopathy, assess related structural and functional cardiac abnormalities, and address further imaging testing to define its etiology. In patients with confirmed cardiomyopathy, echocardiography is the most frequently used imaging technique to stage the disease, to obtain important parameters that facilitate risk stratification and prognosis evaluation, and to detect complications (e.g. intracardiac thrombosis).

In addition to the conventional two-dimensional and Doppler techniques, new echocardiography techniques such as speckle-tracking echocardiography, three-dimensional echocardiography, and intracardiac flow dynamic assessment have opened new opportunities for a more accurate and reproducible assessment of the involvement of various cardiac structure and better understanding of the pathophysiology of cardiac dysfunction.

Using these new echocardiography techniques, we have learned more and more about the importance of the left atrium and the right ventricle in determining the functional capacity and the prognosis of patients with cardiomyopathy.

Clinical application of stress echo in cardiovascular disease

應激性心臟超音波於心血管疾病的臨床應用

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Resting echocardiography is a convenient tool to evaluate cardiac function and provides the mechanism for patients' symptom and sign. However, cardiovascular symptom could be induced by increasing workload or stress because increase in oxygen demand cannot be adequately met by the underlying disease. Therefore, echocardiography performed with stress is able to disclose additional abnormality which might not be seen at rest.

Stress echocardiography is usually performed with exercise, the administration of a pharmacologic agent or atrial pacing. The most common indication of stress echocardiography is evaluation of coronary artery disease. However, stress echocardiography is also helpful in evaluation of hemodynamic status, such as in valvular heart disease, pulmonary hypertension, exertional dyspnea and left ventricular filling pressure. In addition, stress echo has advantage of assessment of myocardial viability and prognosis as well.

With the use of the regional wall motion abnormality criteria, the sensitivity and specificity of stress echocardiography are comparable to stress thallium. However, the diagnostic accuracy depends on the patient population, the expertise of the interpreter, and the quality of the imagines.

We will primarily discuss the use of stress echocardiography using 2D, 3D and strain echocardiography in daily practice.

The past, present and future of **3**D echocardiography in coronary artery disease

過去，現在及未來三維超音波影像於冠心病的應用

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After the advent of matrix array 3D transducer, transthoracic 3D echocardiographic assessment of coronary artery disease (CAD) has been steadily advancing. I will present the past, present and future of 3D echocardiography (3DE) in CAD.

Past: Since 3DE datasets encompass whole part of the left ventricular (LV) myocardium, it has a potential for comprehensive assessment of regional wall motion during stress echocardiography. 3DE requires only one data acquisition in contrast to multiple data acquisition of 2D echocardiography (2DE). Multiple short-views are extracted from full-volume 3DE datasets. Three (two) standard apical long-axis views are also simultaneously recorded using multi-plane (bi-plane) mode. Several authors have investigated the diagnostic accuracy of 3DE stress echocardiography. However, reported accuracy was not superior to that of 2DE stress echocardiography partly because 3DE had a limited temporal and special resolution, and assessment of regional wall motion was still subjective.

Present: 3D speckle tracking analysis provides global and regional strain in multiple directions, thus allows to provide objective information of LV myocardial function. 3D deformation parameters, which reflect regional and global LV function, may reliably evaluate infarct size and transmural extent of myocardial infarction. Several studies have demonstrated the clinical usefulness of 3D strain analysis in patients with acute myocardial infarction, who underwent primary percutaneous coronary intervention. Other studies have investigated the diagnostic value of 3D strain measurements for evaluating the transmurality of infarction, which was verified using cardiac magnetic resonance with late gadolinium enhancement. Potential value of 3D strain to determine myocardial infarct size has been also reported. Summarizing these results suggest that regional and global 3D strain analysis may be useful to estimate the transmural extent of myocardial infarction and to predict LV adverse remodeling. However, 3D strain measurement is not sufficiently sensitive to discriminate between subendocardial infarction and transmural infarction. Finally, global 3D strain values are not useful to determine infarct size. There are also no consistent findings to suggest that 3D strain is more useful than 2D strain. Further large-scale studies are required to determine whether 3D strain has some added value over 2D strain for evaluating patients with CAD.

Future: Multimodality imaging allows to make fusion imaging. Some authors performed fusion imaging using computed tomography coronary angiography (CTCA) and 3D longitudinal strain. Their results suggest that fusion imaging with 3D strain and CTCA provide valuable information to detect functionally significant coronary stenosis, even at rest.

Conclusion: 3DE datasets with 3D LV speckle tracking software provide LV volumes, LV ejection fraction, and 3D global strains with multiple directions simultaneously. In addition to facilitating further refinements of both 3DE image quality and 3D LV strain software, application of fully-automated 3D strain software may expand its adoption for the evaluation of CAD.

Imaging guided PCI for left main bifurcation lesions: How to use IVUS and OCT

血管內超音波及光學斷層掃描影像導引經皮冠狀動脈治療左主動脈幹分叉病灶

Takashi Akasaka

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Recent guideline demonstrated class I or IIa recommendation for left main (LM) percutaneous coronary intervention (PCI) in cases with low or intermediate SYNTAX scores, respectively, based on the recent studies which are showing that there are no significant differences in the prognosis and major adverse cardiac events (MACE) between PCI and coronary artery bypass graft (CABG) for LM disease if the SYNTAX score is low or intermediate. However, LM bifurcation PCI is thought to be still challenging to obtain optimal results and to reduce MACE compared with CABG in cases with LM bifurcation lesion. Compared with angio-guided, intravascular ultrasound (IVUS) guided LM bifurcation PCI has demonstrated better prognosis and less MACE in several trials because minimum stent area (MSA) should be bigger in IVUS guide compared with angio-guide and optimal results could be expected by IVUS guidance. Based on these reports, certain cut-off values of MSA for LM, polygon, proximal left anterior descending artery (LAD) and left circumflex artery (LCx) have been recommended for predicting in-stent restenosis in Asian people.

Recent pilot studies using 3-D optical coherence tomography (OCT) guided PCI for LM bifurcation have reported that stent struts condition and guide wire position at the bifurcation can be identified automatically as virtual images and much more precise treatment could be performed compared with IVUS guidance, and improvement of the prognosis could be expected by OCT guidance because of higher resolution with high frame rate, auto-measurement systems, 3-D reconstruction, etc.

Thus, present status of imaging guidance for LM bifurcation PCI would be demonstrated, and future perspectives of it would be discussed in detail in this presentation.

Intravascular imaging assessment in CAD

冠心症的血管內超音波影像評估

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Since the late 1950's, the "gold standard" for the diagnosis of coronary disease has been the angiogram. The tremendous utility of the coronary angiogram comes from its ability to provide an overall map of the distribution of the coronary arteries and the location of atherosclerotic narrowing.

This situation has changed dramatically in the last decade with advances in our understanding of the pathogenesis of coronary artery disease and the development of minimally invasive, lesion-specific treatments such as balloon angioplasty. It was proliferation of balloon angioplasty and other catheter-based therapies in the 1980's that motivated the development of intravascular ultrasound. Ultrasound imaging from inside the artery seemed to be an ideal choice for detailed visualization of plaque morphology and composition, given the ability of ultrasound to penetrate through the vessel and show the plaque in a cross-sectional or tomographic format. The cross-sectional images of coronary arteries from intravascular ultrasound provide a precise characterization of the location and extent of plaque within the arterial wall. The most striking difference between the images from intravascular ultrasound and angiography is the tremendous extent of plaque burden shown by ultrasound that is not evident on the angiogram

The strongest clinical role for intravascular ultrasound is in the monitoring and guidance of catheter-based coronary interventions. Ultrasound has provided new information concerning the mechanisms of balloon angioplasty and new insights concerning the long-term outcomes of the procedure.

Intravascular ultrasound is established as a new standard for the visualization and measurement of coronary atherosclerosis in living patients. The ability to observe the disease process directly with ultrasound will provide the basis for a number of key studies evaluating ways to treat atherosclerotic plaque both pharmacologically and with new catheter-based techniques. In the meantime, intravascular ultrasound is being utilized on a day-to-day basis in many catheterization laboratories to monitor and optimize existing coronary procedures. In the process, cardiologists are able to view the procedures they are performing with a new level of insight and understanding.

Angiography-derived functional assessments in coronary artery disease

血管造影術在冠狀動脈疾病的生理功能評估

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Coronary angiography is the current standard of care to evaluate the anatomical severity of obstructive coronary artery disease. Myocardial ischemia is considered the cornerstone of the treatment of patients with coronary artery disease. However, it has been known that there is mismatch between coronary anatomy and physiology. Current Guidelines on coronary revascularization suggest that fractional flow reserve (FFR) measurement is indicated for the assessment of the functional consequences of moderate coronary stenosis. Likewise, it has been demonstrated that FFR-guided revascularization strategy is associated with a favorable long-term outcome with decreased major adverse cardiovascular event. Nevertheless, the adoption and penetration rate of FFR measurement remain low in clinical practice which may be attributed to the limitations of FFR (e.g. invasive wire-based approach, maximal hyperemia required…etc.).

Currently, coronary functional assessment can be performed without maximal hyperemia and pressure wire. Several dedicated softwares (e.g. QFR, vFFR and FFRangio) can assess coronary physiology based on computational fluid dynamics and three-dimensional reconstruction model and provide information to guide coronary intervention. This angiography-derived functional assessment may be incorporated in the Cath Laboratory easier than invasive wire-based FFR measurement in the treatment of coronary artery disease.

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兒科醫學之新進展

Recent Advances in Pediatrics

時 間：109年6月6日 08:30~17:30

Time：June 6, 2020 08:30~17:30

地 點：臺北榮民總醫院 致德樓第三會議室

Place：The Third Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

兒科醫學之新進展
Recent Advances in Pediatrics

Development of a gene therapy for Fabry disease

發展法布瑞氏症基因治療技術

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Fabry disease (FD) is an X-linked lysosomal storage disease, which is caused by genetic mutations on human GLA gene that encoded alpha-galactosidase A enzyme. The incidence of FD was around 1/50,000 worldwide, but relatively higher at approximately 1/1,471 in Taiwan. The biological function of GLA is involved in the breakdown of globotriaosylceramide (Gb3) in lysosome. Lack of GLA enzyme activity resulted in accumulation of Gb3 and caused life-threatening diseases such as stroke, cardiac, and renal failure. The enzyme replacement therapy (ERT) is the most common therapy for FD. However, ERT has several disadvantages, such as short half-life of protein drug and extremely expensive. Therefore, development of a new therapeutic strategy for FD is highly demanded. The gene therapy using adeno-associated virus (AAV) vectors may be a promising therapeutic approach. We developed AAV8 and AAV9 viral vector encoding GLA and applied to Gla knockout (Gla−/y) mice, a model of FD. Enzyme activity, the clearance of Gb3 accumulation, immunogenicity and proteinuria symptom were examined to investigate its therapeutic effect in treatment to FD mice model. Our results showed that the GLA enzyme activity was significantly higher in plasma, liver, heart and kidney of FD mice after treated with AAV9-GLA than those treated with AAV8-GLA. We had also determined that enzyme activity can sustain for at least 3 months. Furthermore, we had found out that both AAV8 and AAV9 groups showed low immunogenicity in FD mice. Moreover, AAV9 group ameliorated proteinuria when compared to untreat groups. Our data demonstrated the therapeutic potential of AAV9 vector–mediated GLA gene therapy for FD. Hopefully, by single administration of AAV gene therapy, we can resolve the inconvenience of repeated injection of ERT and improve patient's life quality. The use of AAV gene therapy may become a new strategy for treating FD.

Outcomes analysis of Pompe disease with ERT: **10**-year cohort study

龐貝氏症：酵素補充療法之十年預後分析

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Pompe disease is an autosomal recessive lysosomal storage disorder characterized by the deficiency of acid α-glucosidase (GAA). Deficiency of this enzyme leads to the progressive accumulation of glycogen in numerous types of cells and tissues. Early enzyme replacement therapy (ERT, Myozyme; Sanofi Genzyme) can prolong survival and improve the long-term outcome of Pompe patients.

Our series jointed nationwide Pompe newborn screening from 2008, testing approximately two-thirds of the newborn population in Taiwan. Until 2020, more than 1.3 million newborns were included in our series. By 2010, we established a rapid diagnostic strategy and almost of our infantileonset Pompe disease (IOPD) patients could receive ERT within 4 hours of admission. Now, the average age of our IOPD patients started their ERT less than 8 days of age, the earliest group all over the world.

We compared many prognostic parameters and showed that our patients who received very early ERT had better outcomes. However, according to our 10-year follow-up, we found that our patients, even having better outcomes in many aspects, still presented some problems.

This study will be the first large-scale cohort study, including total 35 infantile-onset and late-onset Pompe patients. We hope that this study could provide the new point to improve the quality of long-term care and might provide a new therapeutic recommendation for Pompe disease.

Early treatment of children with Spinal Muscular Atrophy: VGHTPE experience

脊髓性肌肉萎縮症兒童的早期治療成果：臺北榮總之經驗

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Spinal muscular atrophy (SMA) is the most common fatal autosomal recessive disorder, with an estimated incidence of 1 in 10,000 live births. The disease is caused by absence of a fully functional motor neuron protein gene that produces the survival motor neuron (SMN) protein. SMN protein encoded by two SMN genes: the SMN1 gene, which is the SMA-determining gene, and SMN2 gene. The newborn screening for SMA in one institute of newborn screening center in Taiwan is reported.

Since SMA newborn screening started from August 2017 at Taipei Institute of Pathology and Chinese Foundation of Health (two of the total 3 important newborn screening centers in Taiwan), several individuals with suspected SMA were found.

Two children, with suspected SMA from newborn screening, were referred to our hospital for diagnosis. MLPA was performed and the results of both showed SMN1 to SMN2 was 0 to 3. They showed regression of motor skill at the age of 5 to 6 months old, and SMA type I was diagnosed. We started an intrathecal spinraza therapy as soon as possible. The follow-up motor assessment, CHOP INTEND and HINE-2, showed a little regression initially and quickly catch-up after treatment. Preserved motor function was noted compared with the other patients who received therapy. No respiratory distress, dysphagia or scoliosis were noted.

In conclusion, the importance of early identification from newborn screening leading to early therapy is crucial in clinical practice. Multidisciplinary teamwork is important for the care and outcome of the patients.

Pediatric inflammatory demyelinating diseases in Taiwan

兒童中樞神經發炎性脫髓鞘疾病之台灣經驗

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Multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) are two major forms of chronic inflammatory demyelinating diseases of central nervous system in childhood. To gain updated information and better understanding of these diseases in Taiwan, we recently carried out a series of descriptive and analytical nationwide epidemiological research using data from National Health Insurance Research Database. We found that the incidence of MS was stationary during 2003-2015, while the prevalence of MS was increasing in adults and stationary in pediatric populations. The incidence and prevalence of pediatric and adult neuromyelitis optica (NMO) were apparently rising during the same period, partly due to better recognition of this clinical entity. Furthermore, our study showed that several autoimmune disorders were associated with differential risks of conversion to MS or NMO after optic neuritis. Overall, the rate of conversion to MS after optic neuritis was much lower in Taiwan compared to that in Caucasian populations. The rates of conversion to MS or NMO after optic neuritis were not significantly different between pediatric and adult populations. In this talk, I will present the results of this series of studies, including the epidemiology and comorbidities of pediatric MS and NMO, as well as the inter-relationships between pediatric optic neuritis, MS, NMO, and canonical autoimmune disorders.

Application of cardiac impedance in critical and non-critical patients

心臟阻抗儀在危重和非危重患者中的應用

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Background: Traditional cardiac impedance, a medical instrument used to monitor critically ill persons, is not a novel and new machine. However, few parameters and unsatisfied signal-noise ratio limited the clinical application. Physioflow is a relatively newer appliance that has lower signal-noise ratio and more monitoring parameters. It can detect stroke volume (SV), stroke volume index (SVI), heart rate (HR), cardiac output (CO), cardiac index (CI), contractility index (CTI), ejection fraction (EF), ventricular ejection time (VET), and early diastolic filling ratio (EDFR) directly. If the blood pressure is available, the end-diastolic volume (EDV), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI), and left cardiac work index (LCWi) can also be obtained.

Methods and Results: During Jan 2018 to May 2020, the patients who agreed to receive Physioflow examination were included in this study. The data was analyzed individually. We will present some interesting cases and discuss the relationship between the data of Physioflow and the clinical conditions.

Conclusion: Physioflow is a good tool to monitor critical patients and high-risk patients continuously. It also can be used in potentially high risk patients with a specific maneuver. Further analysis is needed before broadening its use in different diseases and individuals.

Recent progress of homograft transplantation

同種血管移植的新進展

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The aim of this presentation is to introduce the core technologies, biophysics and bioengineering results of the stem cell small caliber vascular tissue graft. Since artificial vessels prove to be a non-optimal medical device, allograft vessels remain an ideal and good standard of vessels. Our team is equipped with extensive experience and has studied cryopreserved homograft heart valve for almost 20 years. We had accomplished animal studies at 1990~1995 and more than 50 homograft tissues had been transplanted successfully by 3 different Veterans General Hospitals and these cases were then tracked for over 12 years. Based on our practical experience on cardiac vascular operating technic and the international certification experience from human tissue Banks, we established a homograft cardiac vascular tissue bank in 2009. The homograft lab has passed the Taiwan food and drug administration (FDA) accreditation and starting clinical usage in August 2011.

The stem cell small caliber vascular tissue graft, which is the cutting edges technology of tissue engineering and translation medicine. In combination of decellularization and recellularization technics, decellularized small caliber vascular scaffold will be recellularized with stem cells (including endothelial progenitor cell and mesenchymal stem cell).

Patient-reported outcomes in survivors of childhood hematologic malignancies with hematopoietic stem cell transplant

兒童血液惡性疾病接受造血幹細胞移植後長期存活者之病患自訴預後 (PRO) 分析

Hsiu-Ju Yen

顏秀如

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臺北榮民總醫院 兒童醫學部 及 國立陽明大學 醫學院

Background: Patient-reported outcomes among survivors of pediatric hematopoietic stem cell transplant (HSCT) are understudied. We compared symptom prevalence, health-related quality of life (HRQOL), and risk factors in adult survivors of childhood hematologic malignancies treated with HSCT to those treated with conventional therapy and non-cancer controls.

Methods: Survivors of childhood hematologic malignancies (HSCT N=112 [70% allogeneic, 30% autologous]; conventionally-treated n=1,106) and non-cancer controls (n=242) from the St. Jude Lifetime Cohort Study completed surveys assessing 10 symptom domains, and SF-36 HRQOL summary scores. Chronic health conditions (CHCs) were validated by clinical assessment.

Results: Multivariable logistic regression reveals that compared to non-cancer controls, HSCT survivors endorsed a significantly higher symptom prevalence in sensation (odds ratio (OR)=4.7, 95% confidence interval (CI)=2.6-8.4), motor/movement (OR=4.3, 95% CI=1.6-11.0), pulmonary (OR=4.6, 95% CI=1.8-11.8) and memory domains (OR=4.8, 95% CI=2.5-9.2), and poorer physical HRQOL (OR=6.9, 95% CI=2.8-17.0). HSCT and conventionally-treated survivors had a similar prevalence of all symptom domains and HRQOL (P's>0.05); however, HSCT survivors had a significantly higher cumulative prevalence for specific symptoms: double vision (p=0.04), very dry eyes (p<0.0001), and trouble seeing when wearing glasses (p<0.0001). Occurrence of organ-specific CHCs, instead of transplant receipt, was significantly associated with a higher prevalence of all symptom domains (p's<0.05) in adult survivors of childhood cancer, except for pain and anxiety domains.

Conclusion: This study found that patient-reported outcomes were equally impaired between HSCT and conventionally-treated survivors, but poorer in both groups compared to non-cancer controls. Poor patient-reported outcomes in all survivors of childhood hematologic malignancies correlated with the presence of CHCs, whether treated with conventional therapy or HSCT.

The prognostic impact of pathological fracture on survival of limb osteosarcoma

病理性骨折對於肢體骨肉瘤預後的影響

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洪君儀

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Background: A multicenter analysis of the prognostic impact of pathological fracture on survival of high-grade osteosarcoma over the extremities is lacking in Taiwan. The purpose of the present study was to determine whether a pathological fracture in an osteosarcoma has prognostic importance and treatment implications.

Methods: In a cooperative effort of the Taiwan Pediatric Oncology Group, members from seventy institutions provided retrospective data on 312 children with osteosarcoma over the extremities who had received pre-operative chemotherapy and tumor excisional surgery were recruited in this study. Demographic data, tumor features, treatment-related factors, and impact on survival of patients were analyzed. Subgroup analyses were performed to compare the features between patients with pathological fracture and no fracture.

Results: In univariate and multivariate analyses, the three factors that significantly influenced overall survival (OS) and event-free survival (EFS) rates were primary metastasis, pathological fracture, and histologic response. The five-year OS and EFS rates were 56.2% and 41.4% for the group with a pathologic fracture, and 74.4% and 58% for the group without a fracture (p = .035 and p = .039 for OS and EFS, respectively). The limb salvage rates in the group with a fracture and without a fracture were 93.3% (42/45) and 91.2% (237/260) (p = .63). In addition to distal femur (48.9%), tumors with pathological fractures were more likely to occur in proximal humerus (22.2%) and proximal femur (13.3%) compared with non-fracture group (p < .01). Patients with pathological fractures had a two-fold higher rate of bone relapse than those without fractures (6.7% vs 2.7%).

Conclusion: Pathological fracture is an independent prognostic factor for osteosarcoma in Taiwanese children. Risk factors that cause pathological fractures should be controlled.

New dimension of the care of childhood kidney diseases: From diagnosis to treatment

兒童腎臟疾病照護的新領域：從診斷到治療

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The care of childhood kidney diseases is important to prevent the development of childhood chronic kidney disease (CKD) and end-stage renal disease (ESRD). The causes of CKD in children are divided into four categories: (1) congenital abnormalities of kidney and urinary tracts (CAKUT); (2) nephritis to ESRD; (3) genetic diseases; (4) caused by nephrotoxic drugs. Early diagnosis and prompt treatment is important in children with kidney disease to prevent progression to CKD and ESRD.

The current treatments of children with kidney disease include controlling the co-morbidities and complications of worsening renal function, and to delay progression of renal function damage. In order to provide deeper understanding of the mechanism and better management of kidney diseases in children, further treatment may focus on personalize precise medicine.

Precision medicine is based on molecular medicine, immunity, physiology, and pathology. Explore the correlation of genetic exposure as a single gene or non-single gene variation, find the correlation of environmental exposure, and based on the physiology and histopathology to find the biomarkers are the important aspects of further research. Ongoing direction will focus on the specific pathway of the biomarker; new therapeutic drugs targeted specific molecules can improve the prognosis.

The goal of care of childhood kidney disease is to confirm the risk factors for the development of novel and traditional kidney disease; to identify the risk factors for kidney function deterioration; to explore the path and key target of childhood kidney disease; and to find the biomarkers to monitor and predict clinical characteristics and prognosis. By precision medicine exploring the genetic, phenotypic, and clinical data will produce novel insights to detect and treat childhood kidney disease, reduce the risk for CKD, and provide ideal therapeutics to reduce the occurrence of ESRD.

Acute kidney injury in childhood-onset lupus nephritis

兒童紅斑性狼瘡腎炎的急性腎損傷

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Systemic lupus erythematosus (SLE) is an autoimmune disease with a wide range of disease manifestations. Childhood-onset systemic lupus erythematosus (cSLE) has been defined as lupus commences prior to 18 years of age. Approximately 15-20% of patients with lupus are cSLE. cSLE is characterized by higher disease activity at presentation, and cSLE are more prone to develop a more aggressive, unpredictable, and relapsing-remitting disease course during puberty. Overall, 50-75% of cSLE have renal involvement. Previous reports showed a 10–30% higher prevalence of lupus nephritis (LN) in cSLE than in adult-onset SLE. Compared to LN in adult-onset SLE, LN in cSLE tends to present early in the disease course and behaves more aggressively. The presentation of LN in cSLE is variable, ranging from asymptomatic urinary findings, nephrotic syndrome, acute kidney injury (AKI), and even chronic renal disease. AKI is a common complication in cSLE with LN. With recent advances in diagnosis and immunosuppressive therapy, the prognosis for children with LN has improved remarkably. Cyclophosphamide, mycophenolate mofetil and azathioprine are reported effective in inducing remission. The role of therapeutic plasma exchange in LN is controversial. Therapeutic plasma exchange may be an adjuvant treatment for patients with severe, refractory disease such as refractory cytopenias, thrombotic micro-angiopathy, severe neurologic involvement and catastrophic antiphospholipid syndrome. AKI in childhood-onset LN is associated with better renal outcome than adult patients. Appropriate therapeutic interventions to achieve remission after induction therapy are highly important for recovery from AKI and long-term preservation of renal function in cSLE with AKI.

Update on COVID-**19**

COVID-**19** 知多少

Miao-Chiu Hung

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SARS-CoV-2 infection, COVID-19, originated from Wuhan, China in Dec 2019, has caused a pandemic with more than 3.8 million confirmed cases and taken at least 265,000 lives by May 10th, 2020. The majority of mortality cases have underlying medical conditions.

It has been reported that children experienced less severe diseases. Surprisingly mild disease course in immunocompromised COVID-19 patients was also noted. The differences of immune response between children and adults triggered by COVID-19 infection have been explored. So far, there is no evidence of vertical transmission while perinatal infection has been reported. Interestingly, BCG vaccination was observed to be correlated to lower mortality rate of CVOID-19 though there is no evidence of causal effect. More studies are ongoing to search for the potential correlation.

Treatment options include chloroquine/hydroxychloroquine, remdesivir, convalescent sera and so on. Anti-IL-6 has been shown to reduce the cytokine storm. Vaccine development is in a race.

The difficulty of infection control lies in its presymptomatic and asymptomatic transmission. The successful experience of Taiwan has been demonstrated to the world.

Implementation and outcomes of a newborn screening protocol for congenital cytomegalovirus infection via saliva samples testing in a tertiary medical center

利用唾液樣本檢測先天性巨細胞病毒感染的新生兒篩檢的執行和成果

Pei-Chen Tsao

曹珮真

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臺北榮民總醫院 兒童醫學部 及 國立陽明大學 醫學系

Congenital Cytomegalovirus (cCMV) infection is the most common cause of non-genetic hearing loss in childhood, which might be underestimated due to the unrecognition of most infected newborns lacking clinical manifestations at birth. We conducted a prospective study of newborn screening for cCMV infection via testing CMV PCR in saliva. Methodology & Theoretical Orientation: Neonates who admitted to our hospital in the period spanning from Mar 2018 to Dec 2019 were enrolled in this study. Dried saliva swabs were collected and investigated for CMV-DNA. Newborns with any of positive screening-results are referred to confirm the diagnosis using urine PCR or cultures. Newborns with confirmed cCMV infection were suggested for scheduled follow-up of auditory function and neurodevelopment evaluation for 2 years. Findings: Of the 1472 newborns in northern Taiwan during study period, nine has positive results of saliva samples. Of positive cases, seven newborns were confirmed cCMV infection and one refused to further study. In 5 cases with discordant findings the discrepancy was due to false-negative (n = 4) or false-positive (n = 1) PCR results in saliva. PCR in saliva showed a positive predictive value of 77.8% compared to urine. The 4 false-negative cases had a significantly lower level of viral load in urine than the 7 cases with concordantly positive results had ($p < 0.0001$; Mann-Whitney test). The incidence of cCMV infection is 0.67%. One case with cCMV infection failed the hearing screening and had diagnosis of mild hearing impairment at 1-month-old. There were 7 cases and 1 cases having auditory and neurodevelopmental evaluation at age of 6 and 12 months. All of these cases had reports of normal performance. Conclusion & Significance: Saliva qPCR is a feasible approach for screening of congenital CMV infection. Newborn screening for asymptomatic cCMV infection might contribute to late-onset auditory and neurological sequelae monitoring and early intervention.

Tracing pathogenic mutations in human populations

追蹤致病基因變異

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Knowledge on the genomics-underpinned human physiology and pathology accumulates quickly in recent years due to the fast advancement of high-throughput genomic technology. Among all technologies available, the single nucleotide polymorphism (SNP) microarrays and the next generation sequencing methods represented two iconic platforms in the 21st century. The former was the major driving technology for genome-wide association studies (GWAS), while the latter can quickly elucidate vast amounts of genomic information for research and clinical purposes.

The next generation sequencing technology was capable of indicating the causative mutations of familial diseases with high-penetrance genetic defects. Several case reports will be presented, including a case study on the Ataxia Telangiectasia disease in a family with a diagnosis of homozygous dysfunctional alleles in the ATM gene in the index patient. This mutation caused a frameshift of amino acid synthesis and a truncated protein which has a reduced length of 1913 amino acids instead of a normal length of 3056 amino acids.

The high density SNP array has been widely used in many GWAS. Yet, the array has more potential in other applications apart from GWAS. Recent studies in Dr. Dau-Ming Niu's team suggested that a pathogenic mutation is responsible for most late-onset Fabry disease patients in Taiwan and Asia. It remained unclear when and where the mutation emerged. Using the decay of Linkage-Disequilibrium, we were able to infer that a founder mutation probably have occurred about 800~ 1068 years ago and spread to different Asian regions by descent.

Total solution of genetic tests for children with development delay

發展遲緩兒童的完整基因檢測解決方法

Yann-Jang Chen

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Developmental delay (DD) is a common pediatric condition, with copy number variations (CNVs) considered one of its major causes. This study aims to determine the efficiency of whole exome sequencing (WES) as a first-tier diagnostic test to detect aberrations including CNVs and single nucleotide variants (SNVs) in comparison with array comparative genomic hybridization (aCGH) for DD.

Subjects (n=541) diagnosed with global developmental delay (GDD) or intellectual disability (ID) of unknown cause have been enrolled, and aCGH tests have a positive rate of 23.7% (111/468). Fragile X syndrome or Rett-like syndrome tests and treatable targeted NGS-based panel were also utilized for assessment. Furthermore, WES was performed on 34 cases with Agilent SureSelect target enrichment system using Illumina HiSeq2000. WES data were analyzed using Varseq v2.1.0 and Illumina BaseSpace Variant Interpreter.

Trio analyses were performed on 24 aCGH-negative cases, thus far revealing 4 known rare pathogenic variants associated with GDD/ID. To determine the consistency in CNV detection between aCGH and WES tests, 10 aCGH-positive singletons were included. CNVs were detected in 11 out of 13 regions using WES. On average, 115 CNVs with p-values<0.01 were called per case. Spans of these CNVs ranged from 119bp to 15Mbp, with duplications accounting for 65.0% of total calls. Approximately 1% (30/2764) of CNVs were drawn for qPCR validation, and 40% (12/30) of the tested CNVs have relative quantities suggestive or indicative of their CNV types.

WES provides comprehensive and high-throughput information with the potential to cut medical expenditures, elevate diagnostic yield, and reduce diagnostic odyssey.

Microbiota and food allergy

腸道菌叢與食物過敏

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The prevalence of food allergy increases gradually over the past decades, which affecting approximately 8% of children and 5% of adults. Food allergy resulted from a defect in immune tolerance. Gut microbiota have been proved to play an important role in developing immune tolerance. On the contrary, dysbiosis play a pivotal role in the development of food allergy in human cohort studies. This dysbiosis usually take place in early life. Gut microbiota are modified by Cesarean section, diet and antibiotic usage, which have been associated with the development of food allergy. Studies from murine models of food allergy have shown that certain Clostridial species protect mice from the development of food allergy. Certain commensal microbes have been tried to prevent or treat allergic symptoms. Metabolites produced from gut microbiota and dietary nutrients may regulate immune tolerance mechanisms. Short chain fatty acids, fermented end products from insoluble fibers by intestinal bacteria, are important metabolites on the protection from food allergy.

Progress in understanding the role of dysbiosis in oral tolerance and food allergy, especially develop in early childhood, provide opportunity to prevent and treat food allergy in the future. Effects, mechanisms and safety of probiotics on interaction of gut microbiota and food allergy need further evaluation.

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小呼吸道功能障礙
在阻塞性氣道疾病的角色

The Role of Small Airway Dysfunction in Obstructive Airway Diseases

時 間：109年6月6日 09:00~11:30

Time：June 6, 2020 09:00~11:30

地 點：臺北榮民總醫院 致德樓第四會議室

Place：The Fourth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

小呼吸道功能障礙在阻塞性氣道疾病的角色

The Role of Small Airway Dysfunction in Obstructive Airway Diseases

Physiology in small airways

小呼吸道生理學

Yi-Han Hsiao

蕭逸函

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Small airways are defined as non-cartilaginous airways with an internal diameter < 2mm from 8-12th generations of airways to the respiratory bronchioles. Emerging evidence showed that small airway dysfunction (SAD) is a common manifestation and associated with poor outcomes in many airway diseases such as asthma or chronic obstructive pulmonary disease (COPD) as well as interstitial lung diseases. A variety of radiological or physiological tests have therefore been proposed as non-invasive surrogate measurements of SAD, including radiological tools such as high-resolution computed tomographic (HRCT), parametric response map (PRM), single photon emission computed tomography (SPECT), positron emission tomography (PET), hyperpolarized helium-3 gas magnetic resonance imaging (3He-MRI); and functional tests such as spirometry, impulse oscillometry (IOS), single breath nitrogen washout (SBNW) or multiple breath nitrogen wash out (MBNW), and body plethsmography. In this presentation, we will have a comprehensive discussion of the physiological function of small airways and the advantages and disadvantages of different tools assessing small airway dysfunction.

Early detection of small airway dysfunction in chronic lung diseases

小呼吸道功能障礙在慢性肺疾病的早期偵測

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Asthma and chronic obstructive pulmonary disease (COPD) are characterized by persistent small airway inflammation and airflow limitation. Early detection of these diseases in patients with respiratory symptoms and preserved pulmonary function (PPF) defined by spirometry is difficult.

Spirometry is an effort-dependent method to diagnose airflow limitation. Forced expiratory flow after expiration of 25%-75% of forced vital capacity ($FEF_{25-75\%}$) is used to evaluate airflow in peripheral airways. However, the reproducibility and comparability of $FEF_{25-75\%}$ is limited if not adjusted for lung volume. Impulse oscillometry (IOS), using sound waves at frequencies from 5 to 35 Hz, can assess respiratory mechanics during spontaneous breathing. When compared to spirometry, IOS is an effort-independent method that is convenient and more sensitive to detect small airway dysfunction (SAD) and correlates with symptoms and disease severity of asthma and COPD.

In this presentation, we will share our recent publication aimed to identify SAD in patients with respiratory symptoms and PPF using IOS. The result showed IOS parameters especially resonant frequency (Fres) had greater sensitivity to detect SAD in patients with PPF when compared to $FEF_{25-75\%}$. Patients with respiratory symptoms and PPF may have SAD that can be diagnosed with IOS in addition to spirometry.

Clinical application of oscillometry in obstructive lung diseases

強迫振盪肺功能在阻塞性肺疾病的角色

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Oscillometry, also known as the forced oscillation technique, is a noninvasive method with which to measure respiratory system resistance and reactance during tidal breathing. The clinical application of oscillometry as a measurement of lung function has progressed with the spread of commercially available devices, and increasing numbers of studies have examined the usefulness of oscillometry in the evaluation or management of obstructive lung diseases, including asthma and COPD. We herein present recent our study.

Fixed airflow obstruction in severe asthma is usually assessed by spirometry. However, the role of oscillometry in severe asthma is unknown. We hypothesized that oscillometry would be useful to diagnose severe asthma and discriminate it from non-severe asthma. The aim of this study was to assess the usefulness of oscillometry in diagnosing severe asthma. Oscillometry was performed in 48 patients with severe asthma and 207 with non-severe asthma. Recursive partitioning analysis was performed to create classification tree. Recursive partitioning analysis identified 4 classes defined by resonant frequency (Fres) and respiratory system resistance at 5 Hz (R5). Class 4 (n = 22: Fres ≥15.04 Hz and 4.47≤ R5 <6.58 $cmH_2O/L/s$) included 16 (73%) patients with severe asthma. In contrast, class 1 (n = 218: Fres <15.04 Hz) included 187 (86%) patients with non-severe asthma. The accuracy of the diagnosis of severe asthma (class 4) was as follows: diagnostic odds ratio, 16.8; 95% confidence interval, 6.1 to 46.0; sensitivity 33.3%; and specificity, 97.1%. The patients in class 4 had lower %FEV1, %FVC, and FEV1/FVC, and higher BMI and YKL-40 than those in class 1. In conclusion, oscillometry may be useful in identifying severe asthma.

Oscillometry is not a surrogate test for spirometry, but should be used complementarily. One of current limitations is the lack of established normative values in different populations and comparability between different devices. Furthermore, data interpretation is often difficult without physiological understanding, which is why confused interpretation, such as the assumption of R5-R20 as small airway function, has disseminated. Finally, there is a need to update the international statement of the technical aspects and clinical use of oscillometry.

Treatment strategies targeting small airway diseases

針對小呼吸道疾病的治療策略

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Small airways were historically considered to be almost irrelevant in chronic airway diseases (CADs), such as asthma, bronchiectasis and chronic obstructive pulmonary disease (COPD), but, in fact, in the past few years we have learned that they are not so “silent”. The awareness of the involvement of small airways in the pathogenesis of CADs is a cornerstone for the management of those diseases, with a particular importance in the not well-controlled patients.

It is now widely established that the inflammatory process affects both proximal and peripheral lung in CADs patients with a real impact on the clinical and therapeutic aspects. Therefore, evaluating the functional and inflammatory impairment of small airways could help to identify the clinical phenotypes and guide the treatment choices.

The success of small airway therapy depends on several factors, but the amount of drug reaching the peripheral lungs plays a substantial role. Therefore, the best therapeutic choice is the one that allows the inhaled drugs to reach the distal airways. The ability is strictly linked to the size of the molecules: the thinner they are, the easier they can reach small airways. Several studies were performed to assess the efficacy of extrafine formulations compared to non-extrafine, starting from inhaled corticosteroids. Several studies showed that extrafine formulations were more effective than non-extrafine in the regulation of functional and inflammatory parameters that reflect small airways impairment, especially in improving acinar ventilation heterogeneity and in reducing regional air trapping.

In this presentation, we focus not only the role of the small airways and their inflammation in the pathophysiological and clinical aspects of CADs, but also the recent advances in treatment of small airway compartment.

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胰臟癌的最新治療

Modern Treatment of Pancreatic Cancer

時 間：109年6月6日 08:30~12:00

Time：June 6, 2020 08:30~12:00

地 點：臺北榮民總醫院 致德樓第五會議室

Place：The Fifth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

課程網址：北區數位學習網→台北榮總→內科部→胃腸肝膽科
→109年中華醫學會年會胰臟癌的最新治療

胰臟癌的最新治療
Modern Treatment of Pancreatic Cancer

Update status of pancreatic cancer surgery

胰臟癌手術的發展現況

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Pancreatic surgery is one of the most challenging task for both general surgeon and patient. Successful pancreas surgery must take into account its retroperitoneal location, proximity to major vascular structures and the unforgiving nature of the gland. In recent years, minimally invasive surgery is undoubtedly the focus of modern surgery and the focus of surgical development. By minimally invasive surgery, patients could get less pain, smaller wounds, less bleeding, and shorter recovery time. Compared with laparoscopic instruments, robotic surgery platforms could achieve more stereoscopic vision and precise dissection and suturing technique, and are increasingly being used in pancreatic surgery. In this article, we would introduce the evolution and preliminary results of minimal invasive surgery of pancreas surgery in Taipei Veteran General Hospital pancreas team.

New trend of radiotherapy in pancreatic cancer

胰臟癌放射治療新趨勢

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Technological advances in the field of radiation oncology have made much progress in the recent decades. Image-guided, surface-guided, or even real-time MR-guided techniques help radiation oncologists visualize anatomy before or right during irradiation. Particle therapy, including proton and carbon ions, enable more conformal dose distribution while reducing radiation exposure of adjacent normal organs. Dose escalation to the target volume, which could theoretically transform to higher tumor control probability, was thus more feasible. Stereotactic Ablative Radiotherapy (SABR) or Stereotactic Body Radiation Therapy (SBRT) shortened treatment course to usually within 1 weeks from protracted course of 6 weeks in the past. For unresectable pancreatic ductal adenocarcinoma (PDAC), recent published single-armed clinical outcomes of novel radiotherapy techniques often achieved median overall survival more than 2 years, doubling from previous results. With advances on radiotherapy and systemic treatment, difference of prognosis between resectable and unresectable PDAC seems to decrease.

Entrectinib in pancreatic cancer

Entrectinib 在胰臟癌的治療

Nai-Jung Chiang

姜乃榕

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Pancreatic cancer (PC) is a disease with high mortality, with overall 5-year survival rate of 6% (range, 2%-9%) approximately. The majority of patients present with locally advanced or metastatic disease initially, however, there is limited specific biomarkers for early diagnosis. Systemic chemotherapy remains as the standard of care for the treatment of metastatic disease, with median overall survival of 12 months roughly. Recently, comprehensive genomic profiling (CGP) of tumor tissue has led to identify potential targets and improve clinical outcome. For PC, one study has demonstrated that nearly one in five patients could be eligible for existing therapies based on genomic alterations such as BRCA mutations, microsatellite instability-high, NTRK fusions, and so on.

The neurotrophic tyrosine receptor kinase (NTRK) 1, 2, and 3 gene fusions lead to the expression of chimeric rearrangements in tropomyosin receptor kinases (TRK) A, B, and C, respectively, with constitutively active kinase function and signaling pathway in a variety of adult and pediatric malignancies. These gene fusions occur in approximately 0.3% of all solid tumors. Although rare, NTRK gene fusions are also to be known as oncogenic drivers in <1% of PC, which also can be detected with the breadth and depth by CGP testing.

Entrectinib is a FDA-approved, CNS-active, potent and selective inhibitor of the TRKA, TRKB, TRKC, ROS1, and ALK. Initial results from an integrated analysis of the Phase I STARTRK-1, Phase II STARTRK-2and ALKA-372-001 trials demonstrated clinical benefit of entrectinib in adults with metastatic or locally solid tumors with NTRK fusion (10 different tumor types). Three PC patients with NTRK fusion were enrolled and two patients had partial response after entrectinib treatment. In addition, entrectinib is well tolerated with a manageable safety profile.

In this talk, we will discuss about some new targets in PC, including of NTRK fusions and corresponding inhibitors to pave the way to personalized treatment.

Genomic profiling opens new insights into pancreatic cancer and may open new treatment options

基因檢測開啟胰臟癌的進一步了解與新治療

Nicolas Martin
Foundation Medicine Pharma International, USA

With a survival rate of only 9 percent at five years, pancreatic cancer is the seventh leading cause of cancer-related deaths worldwide. With only a handful of targeted therapies food and drug administration (FDA) approved for this cancer type, there is an important unmet need to discover new therapeutic options for these patients. In the last couple of years genomic profiling, such as the service provided by Foundation Medicine, has brought new insights into the genomic alteration landscape of this cancer. KRAS, TP53, CDKN2A, and SMAD4 are among the most frequently altered genes. Microsatellite instability (MSI)-high and/or Tumor mutation burden (TMB)-high phenotypes not often detected (~0.5% of samples). Overall about 25% of pancreatic patients have actionable mutation and those who receive match therapy have a significantly longer median overall survival.

Precision medicine in pancreatic cancer

胰臟癌的精準醫學

Do-Youn Oh

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Pancreatic cancer is projected to be the third leading cause of cancer-related death by 2030. Multiple factors contribute to this dismal prognosis, including late diagnosis, treatment resistance and lack of personalized treatment stratification so far. Mutational landscape of pancreatic cancer is being uncovered. KRAS, ROBO-SLIT pathway, RNA Processing, cell cycle, DNA repair, transforming growth factor (TGR) beta signaling, NOTCH signaling, WNT signaling, chromatin, and SWI/SNF alteration are the important categories of this molecular changes. With the development of tumor biology and precision medicine methodology, pancreatic ductal adenocarcinoma is being subtyped, such as Collisson's subtype, Moffitt's subtype, Bailey's subtype, etc. The translation of these molecular classifications into clinical practice could help the realization of precision medicine in pancreatic cancer.

Parallel with recent successes with cytotoxics (nab-paclitaxel, nanoliposomal irinotecan), interesting therapeutic targets have been emerged in pancreatic cancer and have been targeted by interesting agents in clinical trials. In germline BRCA mutant pancreatic cancer, olaparib, poly (ADP-ribose) polymerase (PARP) inhibitor, has improved progression-free survival as used for maintenance treatment after platinum-based chemotherapy. This is the first success of precision medicine in pancreatic cancer.

The idea of harnessing immune cells to fight cancer is not new, but only recently have scientist amassed enough clinical data to demonstrate what a game-changer cancer immunotherapy can be. Immuno-oncology agents are also being tested in pancreatic cancer.

The evolving treatment landscape of metastatic pancreatic cancer

轉移性胰臟癌的最新治療

Stephen L. Chan
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Over the past two decades, drug treatment for metastatic pancreatic cancer has advanced gradually from monotherapy gemcitabine to availability of a number of combinational regimens. Sequential 2nd line or even third line treatment has been increasingly practised, which contributes to improvement of overall survivals. Recent POLO clinical trial data have opened an area of personalized treatment in pancreatic cancer with the use of maintenance PARP inhibitors after first-line platinum-based chemotherapy in patients with germline BRCA mutations. In the lecture, I shall briefly go over the history of drug development for pancreatic cancer followed by highlighting landmark clinical trials on drug treatment for pancreatic cancer. The talk will finish with case sharing on successful downstage after effective drug treatment.

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智慧醫院病理檢驗之最新進展：臺北榮總經驗

Pathology and Laboratory Medicine in the Smart Hospital: Taipei Veterans General Hospital Experience

時 間：109年6月6日 08:20~12:00

Time: June 6, 2020 08:20~12:00

地 點：臺北榮民總醫院 致德樓第六七會議室

Place: The Conference Room 67, Chih-Teh Building
Taipei Veterans General Hospital

智慧醫院病理檢驗之最新進展：臺北榮總經驗

Pathology and Laboratory Medicine in the Smart Hospital: Taipei Veterans General Hospital Experience

Making the elephant dance: Optimizing laboratory efficiency and quality through smart automation

讓大象跳舞：自動智能化實驗室優化檢驗效能與品質

Hsiang-Ling Ho

何祥齡

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Taipei Veterans General Hospital is an international first-class medical center which has 2,800 beds and more than 8,800 outpatient visits per day. Our laboratory in the Department of Pathology and Laboratory Medicine provides hematology, chemistry, coagulation and urine tests on routine and STAT basis, and perform approximately one million clinical tests annually. To fulfill an increasing demand of clinical tests with higher quality and faster turnaround time (TAT), we recently implemented a series of breakthrough systems from pre-analytical, analytical to post-analytical phases, including automatic phlebotomy assistance system, specimen sorting and transportation system, and total laboratory automation (TLA) system, by which we attempted to establish an automatic smart laboratory. For outpatient phlebotomy service, after introducing the phlebotomy assistance system, we reduced the waiting time for blood-drawing from 40 min to less than 10 min in peak hours. We developed an innovative specimen delivery system by combining TEMPUS600 PTS with mechanical arms, which could automatically, immediately and continuously transport blood samples from the phlebotomy center to our 500-meter away central laboratory within 5 min without any need of manual handling. We also built the specimen sorting and transportation conveyors, which could automatically transfer inpatient specimens from reception counter to the pre-analytical system of TLA within 5 min. Moreover, in the emergency phlebotomy room, the pneumatic tube transfer system with auto-unloading function was installed, which takes less than 80 seconds transferring urgent specimens from the emergency department to the pre-analytical module of TLA in the central laboratory. For total laboratory automation, we integrated both routine and STAT immunochemistry testing in the Cobas series automatic workflow system, which has the highest testing capacity in Taiwan. The average TAT is 15.6 min for STAT tests and 65 min for routine tests. Furthermore, by integrating different instrumentation systems with information technology, we are also able to automatically perform many different types of operation, such as reflex and add-on testing as well as real-time specimen tracking.

In conclusion, through cross-division team collaboration to incorporate various transportation and analysis systems together with integrated connections operated with information technology, we have successfully established a state-of-the-art automation system to optimize our efficiency and quality of laboratory tests in a medical center of Taiwan.

Establishing a smart tracking system for pathology specimens: TVGH experience

智慧病理追蹤系統建置：臺北榮總經驗

Chuan-Po Lee

李傳博

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The processing of pathology specimen is traditionally manual because of the great variety of shape and size of the specimen and the complex methods involved. Monitoring of the process is heavily dependent on paper records, including specimen accessioning, grossing, tissue processing, embedding, sectioning, staining, slide distribution, reporting, and cassette and slide archiving. To manage and evaluate these manual work and paper record is very time-consuming and laborious. Turnaround time monitoring is typically limited to one parameter: accessioning-to-reporting time. Specimen mislabeling is another potential disadvantage; the College of American Pathologists' Q-probe Study quantified mislabeling rates across 136 institutions at 0.11% for cases, 0.1% for specimens, 0.17% for blocks, and 0.11% for slides. If novel sample tracking measures can be implemented, an estimated 89% decrease in total error can be achieved, as reported by Yale School of Medicine (CT, USA).

In order to improve service quality and to comply with updated medical center accreditation requirement, we at Taipei Veterans General Hospital Department of Pathology and Laboratory Medicine initiated a re-engineering of our pathology service process in 2019. We aimed to digitize the tracking system of our workflow, beginning with embedding barcode printer and slide labelling machine to specimen-processing workstations. The laboratory information system (LIS) was also re-designed to integrate with the new hardware and to enable tracking at every step. The optimized workflow is expected to reduce error, improve efficiency, save time and labor, and provide the management team with new information for quality control and improvement. In this seminar, we will demonstrate the opportunities and challenges we encountered along this ongoing process.

Step-by-Step: Department-wide deployment of digital image system for primary pathology diagnosis

臺北榮總病理部全面應用數位影像於日常病理診斷之推動進程

Wen-Yih Liang

梁文議

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臺北榮民總醫院 病理檢驗部

Nearly one year after the United States Food and Drug Administration (USFDA) cleared the Philips IntelliSite Pathology Solution for primary diagnosis, more and more innovative pathology labs are utilizing 100-percent digital images for their daily pathology workload. But large-scale adoption throughout the world may still require a few remaining solutions and improvements, among them next-generation scanning systems, improved viewing software, solid infrastructure, and a showdown between an open- versus a closed-system approach. Full acceptance of the power of artificial intelligence could well be the biggest push of all.

In last September, we had installed the Philips IntelliSite Pathology Solution in our department. This is the first Taiwan Food and Drug Administration (TFDA)-approved system for in vitro diagnosis (IVD), and we have used the whole slide imaging system for primary pathology diagnosis of thousands of cases since then.

In this section, we will introduce our experience in the implementation of digital images in pathology practices, including teleconsultation, slide archiving, tumor board discussion, quality control and education. Finally, we will share our experience of using digital slides for primary diagnosis and artificial intelligence (AI)-assisted diagnosis.

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智慧居家醫療新進展：
聰明用藥、智慧管理、視訊診療

Advance in Homecare: Smart Medication, Smart Self-Care and Teleconsultation

台北榮總居家護理所家家好論壇
蘭嶼雅布書卡嫩居家護理所視訊聯播

時　間：109年6月6日　08:30~12:00
Time：June 6, 2020　08:30~12:00

地　點：臺北榮民總醫院 致德樓第八九會議室
Place：The Conference Room 89, Chih-Teh Building
Taipei Veterans General Hospital

智慧居家醫療新進展：聰明用藥、智慧管理、視訊診療

Advance in Homecare: Smart Medication, Smart Self-Care and Teleconsultation

Advance in smart remote monitor and management of heart failure for homecare patients

居家醫療心臟遠距智慧監測與藥物控制最新進展

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Heart failure (HF) had a significant impact on patients' quality of life and added the complexity of homecare patients. When home care patients with multiple medical conditions including HF are discharged from the hospital, a broad spectrum of adverse events could happen and resulted in subsequent rehospitalization and mortality.

Home health care is increasingly used by heart failure patients and had shown the potentials in their long-term assistance. Successful home care for heart failure patients requires a series of specific interventions from risk stratifying, customized medication, and self-monitoring. This session will provide an overview of recent advances in home-based interventions for patients with HF showed potential in reducing hospitalizations and resulting improvement in health outcomes and healthcare value.

Advance in continuity of medication safety: Smart medication management for patients and homecare in Taipei Veterans General Hospital

持續照護用藥安全新進展：台北榮總居家智慧用藥管理

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Medication errors could occur during transition of care, which may lead to excessive adverse events and mortalities. It is believed that at least half of homecare patients had problems in their daily medication. Medication reconciliation, checking the patient's actual medication use with his medication orders, has great potential for medical staff solving drug-related problems leads to medical errors, unplanned admissions, and unexpected death. However, the effect of medication reconciliation is usually suboptimal in real-world for its huge cost of human power thus limited its practical use.

The current research on applying information technology showed potential in improving medication safety for continuity care. This session will provide an overview of recent advances in medication management. We will present our experience in smart medication management at Taipei Veterans General Hospital.

Control of blood glucose for tube feeding homecare patients and advance in self-monitoring for blood glucose

居家病患管灌飲食者血糖控制以及自我檢測血糖之新進展

Harn-Shen Chen

陳涵栩

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As diabetes is the second most diagnosis leading to the use of home health care, improving diabetes management is an important focus of many home care agencies given their high numbers of patients with diabetes. Suboptimal glycemic control for home care patients leads to excessive readmissions or even mortalities because of hypoglycemic or hyperglycemic episodes. In Taiwan, a large portion of home care patients was multiple comorbid with enteral tube feeding which made glycemic control more challenging for these patients.

Individualized glycemic control programs with self-monitoring may help to optimize glycemic control at home. Recent researches suggested that connected devices allowing people with diabetes to monitor their blood glucose levels remotely with data visualization may improve self-care behavior in diabetes management. This session will provide an overview of update glycemic control and updates of technology-facilitated monitoring programs for diabetes home care patients with tubal feeding.

Broaden the scope of wound care in the Digital Era: What could telemedicine and artificial intelligence bring change in wound care to us?

數位時代創新思維：人工智慧與視訊醫療在傷口照護帶來的新改變

Chih-Hsun Lin

林之勛

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臺北榮民總醫院 外科部 整形外科

Chronic wounds could severely compromise quality-of-life in the patients and always bring a challenge to the caregivers. The total cost of chronic wound care is a burden in medical economy and is getting higher as the aging society comes. Although there is advancement in the knowledge of wound healing, wound dressing, wound therapy and wound care, the pathways to delivery these technologies are still behind. Thus, our department try to incorporate the telemedicine and artificial intelligence to overcome the current dilemma in chronic wound care and try to improve care quality. The aim is to develop a model of integrated, effective and efficient wound care system.

First, Telemedicine 2.0 system is a concept of mobile medical service in wound care (teleACT). The system uses telecommunication technology to integrate nursing home care and hospital. Since Jan, 2019, we introduced teleACT model in evaluation of wound condition. The wounds were categorized into 1. Stable and 2. Requirement of transfer to hospital. For a population of 300 in nursing home care, we found the incidence of chronic wound is about 15.7% (n=47, 95% confidence interval (CI): 11.6-19.8%). Of these 47, the chronic wounds of 11 patients poorly progressed and required hospital assistance (n=11, 95% CI, 11.3-35.5%). 10 patients received the care of teleACT system between nursing home care and chronic wound center. One patient admitted through green pathway. Overall, these 11 patients had successful wound healing finally (wound healing rate 100%). The teleACT system could assist wound healing and reduce hospitalization.

Second, we developed an artificial intelligence (AI) program for assisting the diagnosis of wound condition. The AI was trained and the program verified by the wound photo database of our hospital. Under the training, the AI could establish its algorithm for wound evaluation. The major goal of the AI wound evaluation program is to assist non-professional medical personals, patients, and families for early warning of wound problems before the deterioration of wound condition. Other effects of AI wound evaluation reside on preventing late wound complications including sepsis, major limb amputation, and death. In addition, this AI system is expected to be integrated with teleACT model and our wound care center to provide a multi-dimensional and high-quality care of chronic wound.

Effectiveness of telemedicine mobile health service model on chronic wound care for homecare patients

遠距行動醫療服務模式於居家護理慢性傷口病人使用成效

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國立陽明大學

Background: Chronic wounds have a profound impact on the quality of life and long-term care society. More than 10% of home care patients will develop pressure ulcers and require follow-up hospital debridement treatment. The overall treatment process takes time and energy and consumes huge resources of the overall medical system. In severe cases, it will lead to death (mortality rate 9.5%), need efficient service model to provide comprehensive care. The Taipei Veterans General Hospital homecare center and the Chronic Wound Care Center develop the Taipei Veterans General Hospital teleACT mobile medical service model (teleACT model) to integrate hospitals and home care services with remote communication technology and continuous wound care from 2019. The purpose of this study is to evaluate the effectiveness of home care nurses using telemedicine services in chronic wounds at home.

Methods: A retrospective study was started in January 2019 to provide chronic wound care at home through a telemedicine service model at the home care unit of Taipei Veterans General Hospital. From the medical history, the time of the chronic wound occurred and size were found. The nurses classified the wound as “general wound” and “critically hospitalized/Referral wounds “to calculate the prevalence of chronic wounds and track the follow-up wound care status of each case. The 95% confidence interval of the binomial distribution was compared with foreign related results.

Results: We followed 300 home care patients with a prevalence rate of chronic wound at 15.7% (n=47, 95% confidence interval 11.6-19.8%), and 23.4% of chronic wounds were evaluated as “severe hospitalization/referral wounds” (n=11, 95% confidence interval 11.3-35.5%). We use home telemedicine through telemedicine services. The vast majority (n=10, 91.7%) were successfully treated at home while the rest one patient referred to debridement through “green channels”.

Conclusion: The telemedicine medical service model is helpful for chronic wound care at home, promotes wound healing and reduces the hospitalization rate of chronic wounds.

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腎臟病的轉譯醫學研究：從基礎到臨床

Translational Research in Kidney Disease: From Bench to Beside

時 間：109年6月6日 08:00~12:00

Time：June 6, 2020 08:00~12:00

地 點：臺北榮民總醫院 致德樓第十會議室

Place：The Tenth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

腎臟病的轉譯醫學研究：從基礎到臨床

Translational Research in Kidney Disease: From Bench to Beside

Macrophage TREM**2** on calcium phosphate crystal-induced phagocytosis and NLRP**3** inflammasome activity

巨噬細胞 TREM**2** 在鈣磷結晶吞噬作用與 NLRP**3** 發炎體的角色

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Patients with advanced chronic kidney disease (CKD) suffer from accelerated cardiovascular calcification, namely, uremic cardiovascular calcification, which accounts for their high cardiovascular morbidity and mortality. Beyond the bone and mineral disturbances, tissue-resident macrophages, as the first-line confronter dealing with the calcified lesion, also play important roles in the pathogenesis and possess diagnostic and prognostic values. Triggering receptors expressed on myeloid cells 2 (TREM2) is a surface receptor that expresses in various types of myeloid cells, in particular, macrophages. We demonstrated that TREM2 membrane protein on the human macrophage directly binds hydroxyapatite (HA), the major component of cardiovascular tissue calcification in uremic patients, to perform the crystal phagocytosis. Furthermore, TREM2-knockout human macrophages (THP-1 cells) are defective in phagocytosis when compared with that of wild-type cells, leading to the downregulation of caspase-1 activity and the alteration of interleukin (IL)-1β and IL-18 secretion. Besides, we found that, upon HA crystal exposure, TREM2-knockout macrophages not only exert more pro-inflammatory properties (NFκB, mature IL-1β) but also secrete more pro-calcifying cytokines (IL-6 and tumor necrosis factor (TNF)-α) than the wild-type cells. Our novel mechanistic findings explain our animal data, showing that TREM2-knockout uremic mice exhibit more deleterious cardiovascular calcifications than the wild-type uremic mice.

Role of native vitamin D in CKD-MBD

原料性維他命 D 在慢性腎病礦物質與骨骼疾病之角色

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As the glomerular filtration rate (GFR) loss in chronic kidney disease (CKD), the disturbed mineral metabolism and bone composition start to change that is known as CKD-mineral bone disease (MBD). CKD-MBD is characterized by: (1) abnormal metabolism of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D; (2) abnormalities in bone turnover, mineralization, volume linear growth or strength; (3) soft-tissue calcifications, either vascular or extra-osseous. CKD-MBD plays a critical role in the pathogenesis of cardiovascular complications in CKD patients.

Vitamin D is a steroid hormone, traditionally known for its role in the regulation of calcium, phosphorus, and bone metabolism. Native (or nutritional) Vitamin D can be derived from dietary sources (D2 and D3) and/or produced in the skin by exposure to UV light (D3). It is 25-hydroxylated in the liver and then undergoes 1-alpha-hydroxylation to its active form, 1,25-dihydroxyvitamin D [1,25(OH)2D], by 1-alpha-hydroxylase (CYP27B1) in the kidney (in the context of normal renal function) as well as in extra-renal sites. 1,25(OH)2D binds to the intracellular vitamin D receptor (VDR) to alter gene transcriptional profiles and mediate downstream effects.

Vitamin D deficiency has a high prevalence in CKD and is implicated in all-cause mortality and morbidity risks. Furthermore, the progression of CKD is accompanied by a gradual decline in 25(OH)D production. Vitamin D deficiency in CKD causes skeletal disorders, such as osteoblast or osteoclast cell defects, bone turnover imbalance, and deterioration of bone quality, and non-skeletal disorders, such as metabolic syndrome, hypertension, immune dysfunction, hyperlipidemia, diabetes, and anemia.

Pharmacological 1,25(OH)2D dose causes hypercalcemia and hyperphosphatemia as well as adynamic bone disorder, which intensifies vascular calcification. Conversely, native vitamin D supplementation reduces the risk of hypercalcemia and hyperphosphatemia, which may play a role in managing bone and cardio–renal health and ultimately reducing mortality in CKD patients. Nevertheless, the combination of native vitamin D and active vitamin D can enhance therapy benefits of CKD-MBD because of extra-renal 1α-hydroxylase activity in parathyroid gland.

Glucose metabolism and insulin sensitivity in kidney disease

腎臟病的葡萄糖代謝與胰島素敏感性

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About 30 years ago, Gerald Reaven, often referred to as the "father of insulin resistance," hypothesized that the inability of the body to process insulin normally led to type 2 diabetes and cardiovascular disease. He also pointed out that certain medical conditions that increase the risk for heart disease, such as high triglycerides, high blood pressure, and elevated blood sugar caused by an inability of insulin to do its job, or insulin resistance. He referred to this condition as metabolic syndrome.

The kidneys remove waste, help regulate blood pressure, in part by controlling sodium levels in the blood, balance fluids and direct the production of red blood cells — We believed they were not directly affected by insulin resistance. New evidence suggests insulin could also have distinct actions in kidney tissue that regulate growth, hypertrophy, as well as microcirculatory and fibrotic pathways which, in turn, impact glomerular filtration, including that governed by tubuloglomerular feedback. However, in clinical practice, it is hard to discern the distinct effects of excess circulating insulin and impaired insulin actions, as exist in the insulin resistance individual, meanwhile, it is also difficult to dissect insulin resistance in the level of individual organ from the traditional homeostatic model assessment-insulin resistance (HOMA-IR) based whole body manner.

In this section, we take a look of diabetic kidney disease (DKD) in a new perspective, digging out the vary basic pathophysiology of DKD from animal models and clinical samples. We'll have a journey starting from the basic cell energy metabolism, through physiological changes after insulin resistance in different nephron segments, to the latest theories of metabolic kidney disease, and hopefully, pointing out some ongoing promising treatment strategies.

From basic research of diabetic nephropathy to discover dawn of clinical translation in Chiayi KDCRT

從糖尿病腎病變的基礎研究到發現臨床應用的曙光

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Diabetic nephropathy is one of leading cause of end-stage renal disease that becomes a tremendous healthcare burden in Taiwan. Dysfunction of mesangial cells and podocytes in renal glomerular micro-compartments contribute to diabetic nephropathy. Compared with conventional mechanisms of diabetic nephropathy, the Dickkopf-1(DKK1)/Wnt/ β-catenin signaling pathway is virgin land in this field. By searching the PubMed at that time (2006), there is no research group in the world studies on molecular mechanism of DKK1/Wnt/GSK-3β/β-catenin signaling pathways that mediated diabetic nephropathy. We have previously demonstrated that excessive fibrosis and apoptosis via DKK1/Wnt pathway in mesangial cells and Notch1 mediated angiogenic reactions in podocytes are important cellular events underlying diabetes-mediated renal injury. Imbalance between Wnt signaling, CB1 and reactive oxygen stress were found to impede homeostasis and function in diabetic renal microenvironments. In another JASN publication, we clearly demonstrated that miR-29a and HDAC4 is an important regulator in the maintenance of podocyte ultra-structure integrity and renal homeostasis. This study highlights an emerging view of an epigenetic mechanism underlying nephrin acetylation in podocytes and suggests that the addition of the miR-29a function is beneficial for improving diabetic podocytopathy. Recently, we have also demonstrated that targeting the KDM6A-KLF10 feedback loop may be beneficial to attenuate diabetes-induced kidney injury. Consistent with the above notion, we also find that levels of either KDM6A and KLF10 proteins or mRNAs are substantially elevated in kidney tissues or in urinary exosomes of human diabetic nephropathy patients as compared with control subjects.

Our research aims to improve patient outcomes. To convert our basic research discoveries into better ways to prevent, diagnose and treat disease, we are using our resources from tissue bank and facilitating linkages between clinical relevant outcome and our laboratory finding, and discovering dawn of clinical translation now, We also are committed to harnessing our advantage to deliver real healthcare improvements in Taiwan.

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耕耘十年展望未來——
全人照護導向的跨領域領導技巧訓練

Training the Leadership of Interprofessional Trainees for Holistic Care-Past & Future

時 間：109年6月6日 08:00~13:00

Time：June 6, 2020 08:00~13:00

地 點：臺北榮民總醫院 科技大樓階梯會議室

Place：Medical Science and Technology Building
Taipei Veterans General Hospital

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New directions in assessment: Current challenges, future trends and innovative practices

臨床教育評估新方向：當前挑戰、未來趨勢和創新作法

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As health professions education continues its evolution towards active learning and competency-based education, assessment has become a rich field for innovations and new practices.

These new approaches towards professional training have rendered many forms of traditional recall-based assessment obsolete both at the under and postgraduate levels.

The COVID-19 pandemic is also having a major influence on educational practices around the world as more institutions increase the proportion of online learning in their curriculum. This has forced educators in the health professions to seek assessment alternatives for learning in online environments.

The purpose of this interactive lecture is to highlight some of the ongoing changes in health professions education, identify emerging challenges in assessment and discuss innovative assessment modalities.

We hope this will be a practical and useful guide for health professions educators, curriculum developers and educational administrators on how to develop better assessment strategies.

High-fidelity simulation stands out! The interprofessional education experience in Tri-Service General Hospital

高擬真訓練在跨領域團隊合作照護脫穎而出：三軍總醫院的經驗分享

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Simulation is an effective teaching method for interprofessional education (IPE). At the end of July 2018, we conducted a high-fidelity simulation IPE, including scenario-simulated film, role-playing with a pre-writing script, healthcare matrix with interprofessional thinking template, evidence-based medicine with shared decision making, and recording the patient's feedback videos in this conference. To improve the course quality, we introduce the Importance-Performance analysis (IPA) to the interprofessional collaborative practice conference (ICPC) held monthly in the Tri-Service General Hospital (TSGH) in Taipei. This study aims to analyze the case and compared the outcome with other session holds in 2018.

The participants were required to complete the Interdisciplinary Education Perception Scale (IEPS) and a 5-question quiz before and after the class via the online interactive app Zuvio. Professions, levels of the profession, previous IPE experience, clinical working experience, and gender were stratified for the outcome. Totally 110 participants completed the real-time pre-post test. Based on the Kirkpatrick model, the level 1, 2a and 2b outcome of the July session showed the greatest average satisfaction (8.97/10), IEPS and quiz improvement rate (4.6% and 27.88%) compared with other months. After stratified with the demographics, the Nursing profession, males, previous IPE experience over 3 times, and clinical working experience 2 to 4 years had better improvement. Totally 1552 respondents completed the importance-performance questionnaire in 2018 with good reliability (Cronbach's alpha > 0.9). Through IPA, the author could compare the distribution in each month and provide improvement suggestions to the ICPC organizing team.

This case study shows the effectiveness of high-fidelity simulation IPE among healthcare students. The high-fidelity simulation IPE in TSGH had a statistically significant positive impact on the audience compared with non-simulated courses based on our case study. The IPA not only provides a novel way to look through the myth of high satisfaction but also helps the ICPC organizing team know their strength and weakness. Further implementation of high-fidelity simulation in IPE should be promoted to other teaching teams in TSGH to provide better IPE and patient care.

Training outcomes of evidence-based holistic care approach for multi-disiplinary teams

全人醫療之實證訓練課程應用於跨領域團隊教學

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During the decades, more and more studies show that the communication between different medical professional is a key factor to affect patient care quality.

Holistic care is a core value of patient care in medical context. To reach this goal, inter-disciplinary collaboration is necessary. For providing effective treatments, the inter-professional cooperation should work together based on Evidence Based Medicine (EBM).

One way to improving communication between each professional is Healthcare Team Resource Management (HTRM).

Shuang-Ho hospital applies HTRM to enhance connection between different professionals. Inter-professional education program has been hold regularly in the hospital and has significant results.

Different forms of educational activities have been hold in Shuang-Ho Hospital. For example, Evidence-based journal club was arranged monthly, discussing a clinical scenario in the meeting with inter-disciplinary participants. Shared decision making (SDM) tutorial is another feature activity. In this speech, the speaker will share his experience in designing the inter-professional education program and teaching to trainees in different level.

Application of virtual reality on the holistic care: Advance care planning as an example

虛擬實境於全人教育的運用：以預立醫療自主計畫為例

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In the recent decade, the concept of advance care planning (ACP) and advance directive (AD) has been widely recognized all over the world. Studies have shown that ACPs improve the quality of end-of-life care and patient and family satisfaction. In Asia, Taiwan has pioneered in this field. The Patient Autonomy Act in Taiwan, the first of its kind in Asia, was first passed in late 2015 and went into effect in 2019.

To promote ACP at the national level, both patients and medical professionals need to be educated about the importance of ACP. Lack of knowledge and confidence regarding ACP is a barrier for medical professionals to discuss ACP with the patients. Besides, in Asian countries, physicians tend to make family-centered decisions, which influence how AD can be implemented. We thus need education tools that fit the local contexts.

Virtual reality (VR) is known for its immersive and interactive simulation experience and can upgrade medical education. As the VR technology advances, it is feasible to engage people in ACP using the VR experience. However, there is no research on how we can apply VR in training the professionals on AD implementation. Therefore, we piloted a study using VR for AD in Taiwan.

We developed a teaching case that helps medical professionals gain a better understanding of ACP and AD. The assessment tools have been integrated into the case. We evaluate if the medical professionals have a more positive attitude toward ACP, more confidence in implementing AD, and behavioral changes related to ACP and AD. Preliminary results suggest a positive educational impact of the VR training.

Technology enhanced leadership training for young physicians

針對年輕的醫師以科技來輔助領導技巧的訓練

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The Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties have jointly identified communication skills as one of the six general competencies for physicians. The Institute of Medicine also specifies communication skills as one of the six essential curricular domains for effective patient care. The U.S. Medical Licensing Examination requires students to take a clinical communication skills examination with standardized patients as part of Step 2. Mini Clinical Evaluation Exercise (Mini-CEX) and Direct Observation of Procedural Skills (DOPS) are used as formative assessments worldwide that demonstrated positive effects on interprofessional medical trainees performance. The importance for teaching and assessment of communication skills had been reinforced by the fact that it had been integrated as one importance domain in mini-CEX and DOPS.

Sometime, treating physicians are lack of enough time during medical encounter for providing detail information about medical procedure to patients and families. Then, medical and dental interns, the least experienced medical trainees, will be the first line interprofessional medical trainees whose will responsible for communication with these anxious patients about details of the forthcoming procedures and treatment. For usability and easy memorization for clinical teachers and trainees, educational committee of our institution has developed the OSCAR (**o**pening, clarify **s**ubject to be discussed, **c**heck patients understanding about the subject, **a**id patient understanding with either written or audiovisual materials, **r**echeck the patients understanding about the subject) framework based on SEGUE structure.

Involvement of medical trainees in patients and families education had been reported to enhance students' self-efficacy in communication and healthcare satisfaction. To enhance patients' and families' satisfaction and maximize information gain, we developed smartphone quick response (QR) codes accessible virtual reality communicational aids for oral cancers treatment, tracheostomy, etc. Until now, In general, medical trainees and their families agreed that the smartphone approachable online materials and OSCAR-based pre-procedural communication meet their help and provided accuracy messages.

The clinical education of interprofessional holistic care

跨領域全人教育訓練實務經驗分享

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Holistic healthcare is a form of healing that considers the whole person—body, mind, spirit and emotions. Holistic care asserts that the patient is a person, not a disease. It's rooted in the understanding that all these aspects affect your overall health, and being unwell in one aspect affects you in others. The goal is to achieve maximum well-being, where everything is functioning the very best that is possible. Providing holistic care means understanding how an illness affects the whole person and how to respond to their specific needs. The important factor to provide holistic care is optimal individual attributes of clinicians. For example, key personal attributes such as sociability, compassion, respectfulness, patient centredness and sensitivity are all thought to facilitate holistic care provision.

Therefore, the topics in this field we can talk about, include ethics, team work, healthcare system, healthcare quality improvement, patient safety, communication skill, medical humanities, infection control, interprofessional education or interprofessional practice, and so on. Some special issues also are included, such as hospice care, gender issue, organ transplantation, discharge plan, long-term care, prevention medicine. The learning methods include exchange-based learning, action-based learning, observation-based learning, simulation-based learning, practice-based learning and others.

Interprofessional education for holistic care and leadership-A to A+

跨領域全人教育與領導技巧訓練 -A to A+

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Within increasingly complex healthcare system, partnership, cooperation, coordination and leadership are important to increase team-efficiency and ensure holistic care by multi-professional team. Healthcare professionals training in holistic care are required to develop a variety clinical skill to facilitate their management of a complex and challenging patient population. Compatibility between personality and profession as well as inter-professional trainees' knowledge are crucial for the success for the provision of holistic care. Skills of history taking, physical examination, effective communication and teamwork are essential for holistic care on psychological, social, and spiritual dimensions.

In view of the great influence of holistic care on treatment, the health-care systems in many countries in recent decades have tried to promote holistic care by applying changes to the educational systems. Facing the challenges of modern healthcare, experts and organizations are demanding physicians have the higher capability for leadership. The Association of American Medical Colleges (AAMC) has called for "new roles for physician leaders" and a "focus on organizational leadership in a new era of healthcare". In graduate medical education, the Accreditation Council for Graduate Medical Education requires residents to demonstrate the ability to "work effectively as a member or leader of a healthcare team or other professional group." The Royal College of Physicians and Surgeons of Canada's CanMEDS physician competency framework includes "Manager" as one of the essential roles of physicians. Leadership has become an essential competency for medical students. Regardless of professional ethics or their field of specialization, physicians play a leading role in the healthcare team and are considered to be ultimately responsible for the overall outcome of patient care. Good medical leadership is the key to building high-quality healthcare. In Miller's framework for assessing clinical competence, the lowest level of the pyramid is knowledge (knows, A), followed by competence (knows how), performance (shows how), and action (does, A+). Today topics focused on training that aiming to boosting medical from A level to A+ level.

Promotion of leadership training and interprofessional education-past and future

跨領域領導技巧培訓模式護理經驗分享

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Interprofessional collaboration is important when providing patient-centered, holistic care. The effectiveness of interprofessional leadership training can enhance the capability of medical professionals to be aware of and integrate their needs, and promote the appropriate care for patients. Through the interprofessionals education (IPE) of leadership skills and medical team work effectively together, by providing patients with the resources and continuous professional training. Interprofessional collaboration may enhance the awareness and attention, to create a culture of IPE among medical workplace, to encourage academic publication and share the clinical experiences. Nurses might take the lead to work with colleagues in other health professionals to aware each others' roles, and the importance of teamwork, communication, and collaboration to provide the high quality and safety of patient care.

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婦產科學高峰學術研討會

The Novel Treatment in OBS & GYN

時 間：109年6月6日 13:30~17:10

Time：June 6, 2020 13:30~17:10

地 點：臺北榮民總醫院 致德樓第四會議室

Place：The Fourth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

婦產科學高峰學術研討會
The Novel Treatment in OBS & GYN

Concepts on the POP management: A revisit

骨盆臟器脫垂處置觀念：再認識

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盧佳序

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Pelvic organ prolapsed (POP) is the descent of one or more of the pelvic organs (bladder, uterus, and vagina) from the normal anatomic location toward or through the vaginal opening. The cause is a loss of pelvic support from multiple factors. A sense and observation of bulging or protrusion in the vagina is the most specific symptom. Evaluation includes a pelvic examination.

Management options on symptomatic prolapse include observation, pelvic floor muscle training, mechanical support (pessaries), and surgery. Pessary use should be considered before surgery in women who have symptomatic prolapse. Traditional vaginal repairs have been used for several decades. There are anterior or posterior repairs, colporrhaphy, uterosacral or sacrospinous vault suspensions. It is easy to perform, with the advantages of being performed through an entirely vaginal approach, requiring relatively short hospital stay and well tolerated. The surgeries use the patient's own tissue for the repair. Although this is a good option, yet it has the higher risk for recurrent prolapse. 20-40 percent of patients may experience return of their prolapse in the future.

When comparing traditional vaginal repairs with sacral colpopexy, the better successful rates of sacral colpopexy are due to the use of a permanent mesh material. In an effort to improve the results of traditional vaginal repairs, mesh began to place vaginally for repair. The results suggested vaginal mesh procedures have the potential to improve the anatomic success rates. And, other advantages include in minimal pain, short hospital stay, and performed quickly. Potential disadvantages include lack of long-term research, possible pain with sexual activity, or problems related to mesh healing.

Better understanding of pelvic functional anatomy, helps in understanding the management of POP. There are various methods of correcting vaginal prolapse via vaginal approach route, and there is no one right answers when to decide which procedure to perform. Being well informed about the surgical procedures and understanding each of their strengths and weaknesses will enable clinicians to select a suitable treatment depending on each patient's desired outcome.

The role of placenta in pregnancy complications

胎盤在妊娠併發症的角色

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Preterm labor is associated with inflammation and infection. Cellular and molecular mechanisms that modulate leukocyte migration and activation at the feto–maternal interface during perinatal infections are unknown. We demonstrated that human placental multipotent mesenchymal stromal cells (hPMSCs) produced IL-8 and IL-6, which attracted neutrophils from circulation to the placental tissue and thus prolonged their life span during infection. We further observed that hPMSCs produced Slit2, which regulated macrophage migration through Robo receptor signaling. The signaling pathways involved in p38 MAPK and Rap1 activation, and the expression of CD11b and CD18 in macrophages. Furthermore, macrophages secreted TNF-α to influence trophoblast inflammasome assembly and decreased trophoblast cell viability. Stearidonic acid and docosahexaenoic acid reduced the macrophage-induced inflammation of trophoblasts by inhibiting inflammasome-related molecule expression and cathepsin S activation.

Poor vascularization was observed in placentas of preeclampsia or intrauterine growth restriction fetuses. We observed that hPMSCs have the endothelial cell differentiation capability and the angiogenesis-promoting potential through interaction with endothelial cells. hPMSCs could be induced to differentiate into endothelial cell with formation of capillary-like structures *in vitro* and *in vivo*, which enhanced the angiogenesis. There is reciprocal signaling between endothelial cells and mural cells derived from hPMSCs. hPMSCs can incorporate into endothelial cells with tube formation and promote endothelial cells forming capillary-like networks than endothelial cells alone. Transplantation of hPMSCs into mouse placentas revealed incorporation of the hPMSCs into vessel walls, which expressed a-smooth muscle actin, calponin, and smooth muscle myosin (heavy chain). hPMSCs express Slit2, which interacts with the Robo1-Robo4 heterodimeric receptor of endothelial cells and enhance endothelial tube formation. Furthermore, we found that paracrine factors containing IL6 cytokines secreted by hPMSCs supported endothelial cell survival through STAT3 and manganese superoxide dismutase activation.

New era in reproductive medicine

生育醫學的新進展

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Good controlled ovarian stimulation results in good outcome. The parameters of body weight, anti-Mullerian hormone (AMH), antral follicle counts, and previous response can assist in the determination of dosage for individual patient. High estradiol level and premature progesterone rise reduce endometrial receptivity. If we plan fresh embryo transfer, it would be important to prevent premature progesterone rise and high estradiol. We determine the time of hCG basing on follicular size, estradiol, progesterone, LH, stimulation duration, and whole profile. VEGF and IL-8 secreted from corpora luteae may play major roles in ovarian hyperstimulation syndrome (OHSS). The hCG induces anti-apoptosis of corpora luteae and VEGF and IL-8 secretion playing major roles in OHSS. For high responders, antagonist protocol (or progestin-primed ovarian stimulation, PPOS), can be used with GnRH agonist trigger and embryo cryopreservation for prevention of OHSS.

Vitrification techniques significantly improve the results of cryopreservation of human oocytes and embryos. The microtubules of meiotic spindles of oocytes are vulnerable to the thermal changes and will depolymerize. After 3 hours of incubation, spindle recuperation is good. Considering both aspects of spindle recovery and oocyte ageing, time schedules for oocyte cryopreservation program make fertilization in the optimal time. Oocyte cryopreservation would importantly contribute to oocyte donation and preservation of fertility for cancer patients or unmarried females.

Preimplantation genetic testing (PGT) is widely used in the prevention of gene diseases and chromosomal abnormalities. More indications have been applied as HLA typing, adult-onset autosomal disease, and cancer predisposition syndrome. PGT-A (aneuploidy) may help to select chromosomal normal embryos and may increase implantation rate, reduce miscarriage, and increase ongoing pregnancy rate per transfer for recurrent miscarriages, repeated implantation failures, advanced maternal age, and single embryo transfer. But it needs more randomized controlled trials to prove efficiency and cost-effectiveness. The strategy of culturing and selecting embryos in the integrated time-lapse monitoring system may improve reproductive outcomes. Whether it is due to the more stable undisturbed culture environment by the time-laps incubator or morphokinetic selection needs further clarification.

Surgery for recurrent epithelial ovarian cancer

復發性卵巢上皮癌的手術治療

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Secondary debulking in women with recurrent epithelial ovarian cancer is widely practiced and debated, which is feasible and safe in selected patients. The results of these studies exist diverse because of various clinical practices and different patient populations. Patients with a positive predictive Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) score who undergo a secondary debulking surgery for platinum-sensitive recurrent ovarian cancer (PSROC) first relapsing after at least six months since platinum chemotherapy experience longer progression-free survival (PFS). AGO DESKTOP I employed a predictive AGO score to identify patients who will have complete tumor resection in secondary surgery, composed of an Eastern Cooperative Oncology Group performance score of 0, complete resection during first-line treatment, and ascites totaling less than 500 ml. Advanced image study, including PET-CT scan, has more positive findings in patients with suspect recurrence who have rising tumor marker levels despite negative results on MRI or CT. They can change the policy by providing precise mapping of the distribution of recurrent disease, and it is associated with a real R0 status after secondary cytoreductive surgery. Besides, secondary debulking increases time to first subsequent therapy and post-recurrence survival in a platinum-sensitive recurrent ovarian cancer patient, especially with $BRCA^{mut}$ candidate for olaparib maintenance after platinum-based chemotherapy. In the era of personalized medicine, the indication of secondary debulking should be individualized. HIPEC following secondary cytoreduction is an alternative approach for patients with recurrent ovarian cancer. A recent meta-analysis showed better OS rates for patients with recurrent ovarian cancer when adding HIPEC to secondary cytoreduction and traditional chemotherapy. Secondary debulking surgery is a clinically beneficial treatment option for selected patients with recurrent platinum-sensitive ovarian cancer. Younger women in good health with a lengthy disease-free interval and isolated tumors are the best candidates for surgery.

Evidence-based prevention and management of preterm birth

從實證醫學看早產的防治

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Preterm birth (PTB) is one of the leading causes of neonatal death and a major risk factor for short- and long-term adverse health outcomes. The rate of preterm birth is increasing in Taiwan for the last two decades. The mechanisms triggering PTB remain unclear, likely due to the heterogeneity of its pathogenesis. Therefore, effective strategies for identifying and treating women with symptoms of preterm labor so as to prevent PTB are crucial. The objective of this talk is to describe, summarize, and discuss the existing evidence on measures of screening and prevention of PTB, and management of women with preterm labor for reducing the risk of PTB.

The application of novel laparoscopic abdominal hysteropexy with absorbable sutures (LAHAS) for women with uterovaginal prolapse

婦女子宮陰道鬆弛手術的新方法：腹腔鏡腹壁子宮懸吊固定手術 (LAHAS)

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Uterovaginal prolapse has a considerable impact on the daily life of the affected women. Traditional or minimally invasive sarcohysteropexy, using mesh for suspension and fixation, remains the golden standard for women with significant symptoms. However, this surgery calls for skillful surgeons and carries some risks of mesh extrusion to the peritoneal cavity and erosion to the bowels. Furthermore, women who undergo the surgery may experience low back and sacral pain due to the fixation on the site of sacrum. Inspired from the past successful experiences of ovarian and uterine suspension with adjustable sutures (OSAS; USAS), herein we describe a novel laparoscopic abdominal hysteropexy with absorbable sutures (LAHAS) for women with symptomatic uterovaginal prolaps, who desire preservation of the uterus. First of all, under laparoscopic inspection, the assistant manipulates the uterus inside until the uterus reaches the anterior abdominal wall to determine the appropriate site, which is marked for subsequent suspension and fixation. Then the pelvic surgeon slices off the top of the uterine fundus to make a rough surface for further adhesion to the anterior abdominal wall. Finally, the remaining part of the uterine fundus is suspended and fixed to the anterior abdominal wall by suturing them together with absorbable stitches. A survey of perioperative and postoperative follow-up reveals comparative results and outcomes. We conclude that LAHAS is an easy, safe, and feasible method that offers benefits for women with uterovaginal prolapse.

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肝硬化及門脈高壓之治療及新知

Liver Cirrhosis and Portal Hypertension: Cure and Beyond

時 間：109年6月6日 14:00~17:00

Time：June 6, 2020 14:00~17:00

地 點：臺北榮民總醫院 致德樓第五會議室

Place：The Fifth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

肝硬化及門脈高壓之治療及新知

Liver Cirrhosis and Portal Hypertension: Cure and Beyond

Recent advance of management of gastric variceal bleeding in patients with liver cirrhosis

肝硬化病患合併胃靜脈出血的新進展

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Gastric variceal bleeding is associated with a mortality rate of up to 20% in patients with cirrhosis. Recurrent gastric variceal bleeding is frequent after initial hemostasis. Gastric variceal obturation via endoscopy is the therapy of choice for acute gastric variceal bleeding but the rebleeding rate is still as high as 65%. A novel therapy for secondary prophylaxis of gastric variceal bleeding is necessary.

Non-selective beta-blockers could prevent variceal bleeding via the mechanism of reducing portal pressure. The beneficial effect is more pronounced in the treatment of esophageal variceal bleeding as an adjunct to endoscopic therapy. However, adding propranolol to endoscopic gastric variceal obturation did not further reduce the rebleeding rate but was associated with more adverse event. Carvedilol is a more potent non-selective beta-blocker than propranolol. A recent randomized control trial also did not find beneficial effect in the patients receiving combination therapy of carvedilol and endoscopic gastric variceal obturation.

Balloon-occluded retrograde transvenous obliteration is a novel therapy for the treatment of gastric variceal bleeding popular in Japan and South Korea. Several observational studies found that balloon-occluded retrograde transvenous obliteration could significantly decrease the rebleeding rate of gastric varices. Nevertheless, balloon-occluded retrograde transvenous obliteration is associated with adverse events including worsening of esophageal varices, jaundice and ascites. Recently, modified balloon-occluded retrograde transvenous obliterations such as plug-assisted retrograde transvenous obliteration and coil-assisted retrograde transvenous obliteration have been developed. Future studies should aim at comparing the efficacy and safety of balloon-occluded retrograde transvenous obliteration with endoscopic gastric variceal obturation.

Relative adrenal insufficiency in liver cirrhosis

肝硬化狀況下之腎上腺功能不足

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The concept of relative adrenal insufficiency (RAI) or critical illness–related corticosteroid insufficiency (CIRCI) has been used to describe a subnormal adrenal response to adrenocorticotropin in severe illness, in which the cortisol levels, even though high in terms of absolute value, are inadequate to control inflammation. Patients with adrenal insufficiency share similar hemodynamic features with cirrhotic patients, namely increased cardiac output, decreased peripheral vascular resistance, decreased mean arterial pressure and hypo-responsiveness to vasopressors. While RAI has been shown in critically ill patients with liver cirrhosis, especially in the settings of septic shock and acute variceal hemorrhage, it also affects non-critically ill cirrhotic patients. The major effect of RAI or CIRCI in critically ill cirrhotic patients is manifested through alterations in the systemic inflammatory response and a blunt response to vasoconstrictors, leading to a further activation of sympathetic nerve system. These effects can worse the hemodynamic impairments in decompensated liver cirrhosis and eventually result in hepatorenal syndrome and multiple organ failure.

The pathophysiology of RAI or CIRCI in liver cirrhosis remains unclear. Inadequate precursor (cholesterol) synthesis and increased levels of cytokine may contribute to impaired adrenal steroidogenesis.

Currently, the diagnosis of RAI or CIRCI should be based on the consensus statements from the American College of Critical Care Medicine, which recommend referring to a delta serum total cortisol after 250 lg corticotropin injection of <9 micogram/dl) or a random total cortisol of <10 micogram/dl).

It is still unknown whether steroid supplement in cirrhotic patients with RAI can improve prognosis.

The impact of incretin therapy on liver cirrhosis and cirrhotic complications

以 Incretin 為主之療法對肝硬化及其併發症之影響

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The incretin hormones, including glucagon-like peptide-1 (GLP-1), are critical to maintain the glucose metabolism. Inhibitors of dipeptidyl peptidase-4 (DPP-4) enhance the effect of GLP-1, which leads to secretion of insulin and reduction of plasma levels of glucose.

Nowadays, GLP-1 analogue and DPP-4 inhibitors have been widely used for the treatment of diabetes mellitus. In addition to lowering blood glucose level, they also exert pleiotropic cardiovascular and anti-inflammatory effects. It has been reported that DPP-4 inhibitor and GLP-1 analogue treatments improved liver fibrosis and inflammation in non-alcoholic fatty liver disease. In addition, emerging evidences showed that GLP-1 analogue treatments improved cirrhotic cardiomyopathy and hepatic microvascular function. Meanwhile, DPP-4 inhibition could alleviate liver fibrosis via suppression of activated hepatic stellate cells. Today, the talk will review the current advances in the relevant field and indeed, the future investigation of incretin therapy on liver cirrhosis and cirrhotic complications is warranted.

The features of gut microbiota in liver cirrhosis and portal hypertension

肝硬化及門脈高壓狀況下之腸道微菌叢的特徵

Pei-Chang Lee
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The gut microbiota is a huge complex of diverse microorganisms that generate various compounds and metabolites, which orchestrate the function of various tissues and organs, especially the liver. Although it has been considered that liver is the “downstream” organ of the gut, the liver and the gut, linked via gut microbiota, influence each other closely. Gut microbiota affect bile acids, choline metabolites, indole derivatives, short chain fatty acids, vitamins, polyamines, lipids, neurotransmitters, neuroactive compounds, and hypothalamic-pituitary-adrenal axis hormones levels, which play major roles in the pathogenesis and regulation of liver cirrhosis and portal hypertension. It has also been demonstrated that dysbiosis in liver cirrhosis leads to fatal complications, such as bacteremia and hepatic encephalopathy associated with small intestinal bacterial overgrowth and increased intestinal permeability. In recent few years, the possibility of ameliorating liver cirrhosis and portal hypertension via the modulation of gut microbiota, including fecal microbiota transplantation, have also been rigorously investigated. This talk, therefore, will focus on the changes and manipulation of gut microbiota in liver cirrhosis and portal hypertension.

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數位科技於牙科應用之現況

Recent Advance in Digital Dentistry

時 間：109年6月6日 13:30~17:30

Time：June 6, 2020 13:30~17:30

地 點：臺北榮民總醫院 致德樓第六七會議室

Place：The Conference Room 67, Chih-Teh Building
Taipei Veterans General Hospital

數位科技於牙科應用之現況
Recent Advance in Digital Dentistry

The current application of digital technology in clinical dental treatment

數位科技於牙科臨床治療應用之現況

Cheng-Han Li
李承翰
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Digital dentistry has been popular in recent years due to increased accuracy and relatively friendly prices. Among all specialties, prosthetic dentistry is the most affected one by digital dentistry at the beginning. Digitalization brings not only an increase in efficiency of making impressions, but also a change in the entire workflow. Especially in chair-side computer-aided design and computer-aided manufacturing (CAD/CAM), the clinical collaboration between dentists and technicians can greatly improve the predictability and efficiency of treatment.

Since last year, digital dentistry has evolved from pure manufacturing to AI computing and process optimization. Manufacturing requires less and less operation, and more and more doctors can be assisted in diagnosis and treatment planning. This allows digital dentistry to step out of prosthetic dentistry.

Using the most advanced technology, we can begin to transfer the wisdom and operation skill to the hands of any dentist in a digital way, so that the most inexperienced dentists can efficiently make high-level and difficult treatments. Since then, the concept of “Collective Wisdom” has entered the field of dentistry. In this speech, I will introduce you to the digital workflow of this new era.

Optimizing functional and cosmetic outcomes in facial reconstruction using computer-aided approaches

電腦輔助設計美觀與功能兼備之顱顏重建

Cheng- Hsien Wu

吳政憲

National Yang-Ming University School of Dentistry, and Oral and Maxillofacial Surgery Section, Department of Stomatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

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The complex nature of the craniomaxillofacial structures challenges the surgeon's knowledge to anatomy, experience, and the perception toward surgical outcome. In head and neck tumor patients, restoring correct facial contour is the key to ensure the functional and esthetic rehabilitation. For the rapid advance of the computational algorithm, we could plan the operation virtually by different computer-aided design tools. Subsequently, the plan is transferred into operation theatre either by surgical navigation system, prefabricated cutting / positioning guides, or the combination of both. By this approach, the operation could be executed precisely, the outcome will be more predictable, and moreover, we may conceal the surgical scar in a minimal invasive way. Nowadays, computer-aid surgery is constantly applied on traumatic, oncologic, and orthognathic cases in our institute and change the daily routine practice profoundly. In this report, I will focus on discussing the application on jaw reconstruction after tumor ablation.

Align your teeth with digital orthodontic technology --- invisible, accurate and ⋯⋯

數位科技帶來的隱形矯正風暴

Tzu-Ying Wu

吳姿瑩

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Digital technology has brought orthodontic tooth aligning and setup into a faster way. Traditional model setup could be virtually planned on computer with 3D view.

Traditional orthodontic appliance could be customized through 3D design and 3D printing technique. Virtual planning could not only help orthodontic treatment plan decision, but also improve the communication between patient and doctor. At the same time, discussion through 3D planning establish a better understanding between doctors in different specialty.

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多發性骨髓瘤在診斷與治療的新近發展

Recent Updates on Diagnosis and Management of Multiple Myeloma

時　間：109年6月6日　　13:20~16:15

Time：June 6, 2020　　13:20~16:15

地　點：臺北榮民總醫院 致德樓第八九會議室

Place：The Conference Room 89, Chih-Teh Building
Taipei Veterans General Hospital

多發性骨髓瘤在診斷與治療的新近發展

Recent Updates on Diagnosis and Management of Multiple Myeloma

Outcome prediction in multiple myeloma

多發性骨髓瘤治療結果之預測

Chieh-Lin Jerry Teng
滕傑林
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臺中榮民總醫院 內科部 血液腫瘤科

Multiple myeloma is a plasma cell neoplasm, which causes monoclonal gammopathy and consequently end-organ damages. The common symptoms include bone pain, nausea, constipation, loss of appetite, fatigue, and weight loss. The outcomes of myeloma patients have improved in the last two decades due to the advance of novel therapies, including proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies, etc. However, there are still a few patients with high-risk features who may have poor outcomes. Factors associated with poor outcomes include patient-related characteristics and tumor-related factors. Although there have been many definitions for high-risk (HR) myeloma, most recent consensus for classifying risk in patients with newly diagnosed multiple myeloma (NDMM) comes from the International Myeloma Working Group. This revised International Staging System includes del(17p) or t(4;14) by fluorescence in situ hybridization, b-2 microglobulin, albumin, and lactate dehydrogenase. These elements should be captured in all NDMM patients. The optimal treatments for HR myeloma have not been fully worked out. Detection of minimal residual disease via the methods of flow cytometry, quantitative PCR and even next generation sequencing (NGS) is attempted to predict the outcome of the patient after active treatment. However, currently, there is no definitive guideline for this application.

The goal of myeloma therapy is to maximize survival time and improve quality of life. Until recently, high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT) is associated with the highest complete remission rate for myeloma patients, and this procedure has been the standard frontline treatment for the younger patients. With the advance of proteasome inhibitors and immunomodulatory drugs, a few studies recently reported that ASCT had no survival benefit compared to the current standard treatment. Whether detection of minimal residual disease (MRD) could help the decision of ASCT is still an open issue.

That is the question: To transplant or not to transplant

多發性骨髓瘤病患是否需要造血幹細胞移植？

Yuan-Bin Yu
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The goal of myeloma therapy is to maximize survival time and improve quality of life. Until recently, high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT) is associated with the highest complete remission rate for myeloma patients, and this procedure has been the standard frontline treatment for the younger patients.

In patients who are eligible for ASCT, induction treatment with bortezomib and an immunomodulatory drug should be administered for 3 to 6 months followed by ASCT. A consolidation/maintenance regimen containing at least 1 year of bortezomib can be given followed by maintenance thereafter. For patients' convenience, an oral agent that is not thalidomide could be prescribed for maintenance therapy. In patients with high risk myeloma, allogeneic stem cell transplantation may be associated with reasonable outcome, but this too will require further research.

With the advance of proteasome inhibitors and immunomodulatory drugs, a few studies recently reported that ASCT had no survival benefit compared to the current standard treatment. Further analysis of those studies will be addressed at presentation.

Treatment updates for relapsed or refractory multiple myeloma

復發或難治多發性骨髓瘤治療的新近發展

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Multiple myeloma is a plasma cell neoplasm, which causes monoclonal gammopathy and consequently end-organ damages. The common symptoms include bone pain, nausea, constipation, loss of appetite, fatigue, and weight loss. The outcomes of myeloma patients have improved in the last two decades due to the advance of novel therapies, including proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies, etc. However, there are still a few patients with high-risk features who may have poor outcomes. Factors associated with poor outcomes include patient-related characteristics and tumor-related factors.

The goal of myeloma therapy is to maximize survival time and improve quality of life. Until recently, high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT) is associated with the highest complete remission rate for myeloma patients, and this procedure has been the standard frontline treatment for the younger patients.

The treatment of multiple myeloma has tremendous advances over the last 10 years. New generations of proteasome inhibitors and immunomodulatory drugs have been approved for patients with relapsed or refractory multiple myeloma. Two types of monoclonal antibodies targeting CD38 and SLAMF7 are also available. A selective inhibitor of nuclear export has been approved to treat triple-refractory patients. Furthermore, clinical trials of Bi-specific T-cell engagers, chimeric antigen receptor T-cell therapies, and antibody-drug conjugates targeting B-cell maturation antigen (BCMA) are ongoing.

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兒童呼吸道手術：創新衍生性研究

Pediatric Airway Surgery: Emerging New Research Topics

時 間：109年6月6日 13:30~17:30

Time：June 6, 2020 13:30~17:30

地 點：臺北榮民總醫院 致德樓第十會議室

Place：The Tenth Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

兒童呼吸道手術：創新衍生性研究
Pediatric Airway Surgery: Emerging New Research Topics

A combination of tracheoplasty and tracheal stenting for treatment of severe congenital tracheobronchial stenosis under ECMO

葉克膜支持下進行氣管成形術合併術後氣管支架置入：臺北榮總之經驗

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劉君恕[a,e] 葉奕廷[a,e] 蔡昕霖[a,e] 吳飛逸[b,e] 宋文舉[d,e] 李昱聲[c,e] 曹佩貞[c,e]

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Background: Congenital tracheobronchial stenosis (CTBS) is a rare congenital condition characterized by complete cartilage rings covering varying lengths of the major airway. In this study, we reviewed the outcomes of patients with CTBS receiving surgical tracheoplasty in our institute.

Methods: We retrospectively analyzed the outcomes of consecutive patients with CTBS operated between 2006 and 2017 when extracorporeal membrane oxygenation (ECMO) was used perioperatively.

Results: In total, 11 patients (median follow-up period, 4.2 years; interquartile range, 1.6–5.4) were included. Seven were symptomatic in the neonatal period, 10 had cardiorespiratory anomalies, 7 required preoperative bronchoscopic balloon dilatation, and 1 required preoperative stent placement. Slide tracheoplasty (STP) was performed in 9 patients, and 2 underwent pericardial patch tracheoplasty. Seven patients required postoperative balloon dilatation, and 6 required postoperative stent placement. Early stenting provided immediate ventilatory improvement in all patients and facilitated successful extubation in a median of 4 days after stenting in 80% of the patients.

Conclusion: Under ECMO, severe CTBS could be successfully treated through a combination of tracheoplasty and bronchoscopic management. STP provided excellent results for solitary trachea stenosis with a minimum diameter of ≥ 3 mm. In selected patients, postoperative tracheobronchial stent placement was crucial in minimizing the ECMO duration and facilitating extubation.

Pediatric interventional flexible bronchoscopy for management of airway disease

以兒童軟式介入性支氣管鏡治療呼吸道疾病

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宋文舉

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Flexible bronchoscopy (FB) allows direct and dynamic inspection of approachable airways.

In pediatric patients FB is mainly used for diagnosis. Pediatric interventional FB (IFB) procedures are difficult to standardize because of the lack of consensus across different medical teams. The main aim of IFB is to keep a patent and wide enough central airway lumens. Current literatures are scant with retrospective case reports or case series s in single center only.

Basic requirement before doing IFB are important which include a secure environment (usually in intensive care unit [ICU] settings), skillful techniques, appropriate instruments, clear airway vision (under bronchoscopy), and well maintenance of cardiopulmonary status of patients. Noninvasive ventilation (NIV) with pharyngeal oxygen with intermittent sustained inflation (by nose-closure) and abdomen-compression (Soong's ventilation) is the preferred method which can be simply performed during IFB by scopist himself. This can provide an effective oxygenation and ventilation supports even in compromised airway with sedation during IFB procedures, without any artificial airways restriction. Bronchoscopists should be trained familiarly in basic IFB procedures such as tracheobronchial intubation, bronchoalveolar biopsy and lavage, balloon dilatation, laser ablation, cryotherapy. Even more advanced and complicated items such as stent placement, maintenance and retrieval are necessary. Especially stent over the left mainstem bronchus or carina region. Frequently, the IFB may require a combination of these techniques. Pulmonologists should achieve and maintain a high knowledge and IFB skill levels during their career. There is a rapidly evolving IFB role in the pediatric ICU care because there are more survivors of critical and cardiopulmonary compromised infants and small children, as well as in the wards or OPD. For keep expertly, IFB procedures require intense practice and a multidisciplinary approach for patient management. With developing technology, the role of IFB is destined to grow.

The IFB modality of using short-length FBs, supported with an NIV and working in an ICU facilities is a viable, instant, and effective management in neonatal and pediatric patients. Successful IFB could result in rapid weaning of respiratory supports without the need for sophisticated transport to the operation theater and more invasive procedures.

Overview: Recent advance of surgical outcome of tracheoplasty in infants with congenital tracheal stenosis

嬰兒先天性氣管狹窄手術氣管成形術之最新進展

Kosaku Maeda

前田貢作

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Background: The aim of the study is to assess the surgical outcome of slide tracheoplasty in patients with congenital tracheal stenosis.

Methods: Pre, intra- and postoperative data were collected. Anatomy and associated anomalies were reviewed.

Results: 49 patients (median age 11 months; range 2month-6 year) underwent surgical correction of congenital tracheal stenosis (slide tracheoplasty:47 and end-to-end anastomosis :2) during period between 2014 and 2018. Associated anomalies were present in 38 patients (78%) including congenital heart disease, left pulmonary artery (LPA) sling, VACTERL (abnormalities of the vertebrae, anus, cardiovascular tree, trachea, esophagus, renal system, and limb buds) syndrome, intestinal atresia, and pulmonary hypoplasia/ agenesis.

Ten patients (20%) needed preoperative ventilation and no needed preoperative extracorporeal membrane oxygenation (ECMO). Median postoperative ventilation was 7 days (5-21 days). Three patients needed postoperative ECMO. Reintubation due to pneumonia and several tracheal dilatations due to recurrent tracheal stenosis, which was eventually stented. There was one hospital death in a patient, who could not be weaned off ECMO due to severe congenital heart disease and diaphragmatic hernia. At a median follow-up of 24 months (3weeks-4 years), all survivors are in good clinical condition and without additional stenting. Risk factors of unsuccess operation are low PaO2, persistent pulmonary hypertension and pulmonary hypoplasia /agenesis.

Conclusion: Slide tracheoplasty can be performed in patients with congenital tracheal stenosis with a good surgical outcome.

Pediatric airway: State of the art

兒童呼吸道最新進展

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許巍鐘

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Pediatric airway problem is usually a life-threatening event for children and always a challenge for pediatric otolaryngologists. The most common congenital and acquired airway problems including laryngomalacia, subglottic stenosis and vocal palsy etc. Since the modern medicine advanced in critical intensive care, and high-resolution video-assisted endoscopy developed, plenty of airway disorders could be managed as earlier as possible, which became the most important part of training in pediatric otorhinolaryngology.

Since 1970s, open airway surgery was popularized and evolved gradually. Specific surgical techniques such as laryngotracheal resection (LTR), cricotracheal resection (CTR) slide tracheoplasy indicated to specific airway pathologies by specific airway surgeons looking for better patient selection by pre-operative evaluation and optimization.

Recently, endoscopic airway surgery has seen a resurgence in the management of pediatric airway problems. In particular, by introducing Laser, microdebrider, coblator, balloon dilation, stenting, and topical injection or tissue fibrin glue application, endoscopic techniques have been widely utilized in the pediatric airway diseases not only for diagnosis but also matured greatly in therapeutic purposes.

Therefore, a more thorough understanding on State of the Art in pediatric airway by integration of endoscopic techniques with open airway surgery is absolutely necessary for pediatric otolaryngologists to more appropriately counsel patients regarding the risks benefits of surgery and expected outcomes of specific techniques.

Children are not small adults. We must treat and look into the pediatric patients as a whole personnel but different from adults because they are still growing. Combine endoscopic techniques and open surgery, considering anatomical correction and respiratory care together, to make more precise options in management of pediatric airway diseases. To gain a better quality of life for both children and family.

Adjuvant pharmacological therapy after airway therapy: Rabbit model

呼吸道處置後的藥物治療：兔動物模型

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Background: Congenital tracheobronchial stenosis is a rare but lethal developmental anomaly of the respiratory tract. The optimal surgical management has evolved over the years and patient survival gradually improved with the advancement of the technique and critical care standards. Dehiscence, granulation, tracheobronchial malacia and recurrent stenosis are still a challenge in the postoperative period. Granulation is the reactive hyperplasia of tissue during epithelial wound healing.

Methods: To evaluate the efficacy of different inhalational regimens and their impact on the histological and immunohistochemistry markers of granulation formation, a well-established rabbit model of tracheal surgery was used. The effects of inhalational azithromycin and ciprofloxacin were compared in additional to inhalational budesonide. Markers of granulation including transforming growth factor (TGF)-β1, vascular endothelial growth factor (VEGF) and matrix metalloproteinase (MMP)-9 were evaluated in addition to histomorphological evaluation.

Results and conclusion: We demonstrate that the current rabbit model is feasible and useful for evaluation of tracheal surgery with postoperative medication intervention. Inhalational antibiotics in addition to steroid may have a suppressive effect on the formation of granulation after surgery.

Computational fluid dynamics in patients with congenital tracheal stenosis

先天性氣管狹窄病患的呼吸道電腦流體動力學分析

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Background: Functional assessment after tracheal reconstruction surgery in infants is not established. We applied computational fluid dynamics (CFD) to the postoperative assessment of pediatric patients with congenital tracheal stenosis (CTS) and aimed to evaluate its validity.

Methods: CFD models were constructed for six patients with CTS before and after slide tracheoplasty and for five infants with a normal airway, using computed tomographic data. Power loss obtained with CFD analysis and clinical respiratory status were evaluated retrospectively.

Results: In patients with CTS, the median power loss was significantly higher before surgery [1.59 (range 0.31-13.6) kPa] than after surgery [0.27 (range 0.065-0.97) kPa]. The median power loss in the infants with a normal airway was 0.17 (range 0.12-0.28) kPa. There was no significant difference with regard to power loss after surgery between the CTS and normal airway groups. Five patients whose postoperative power loss was less than 0.3 kPa had minimal respiratory symptoms. One patient whose postoperative power loss was 0.97 kPa had severe dyspnea.

Conclusion: Postoperative power loss measured by CFD assessment represents clinical severity. CFD analysis can serve as a useful evaluation method in patients with CTS after slide tracheoplasty.

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功能性泌尿學的新進展

New Frontier in Functional Urolgy

時 間：109年6月6日 13:30~17:30

Time：June 6, 2020 13:30~17:30

地 點：臺北榮民總醫院 科技大樓一樓會議室

Place：Medical Science and Technology Building
Taipei Veterans General Hospital

功能性泌尿學的新進展
New Frontier in Functional Urolgy

Surgical tips of male sling application for the treatment of urine incontinence

治療男性尿失禁之尿道懸吊手術技巧探討

Thomas Y. Hsueh

薛又仁

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Prostate cancer is the 5th common cancer in Taiwanese men. For patients with localized prostate cancer, robotic radical prostatectomy is the treatment of choice among most patients. However, post-operative urine incontinence and sexual dysfunction remain the most common complications among patients received radical surgery. The management of male incontinence includes life style adjustment, oral anticholinergic agents and surgical interventions. This review aims to describe a step-by-step illustration of the application of retro public male sling procedures. The tips and tricks of retropublic sling adjustment will be discussed in each step so as to provide a panoramic scheme regarding intra-operative trouble shooting, peri-operative concern and post-operative clinical care. A consecutive case analysis and 2-year follow up data will also be discussed in this review. The most common early postoperative complication is urinary retention but long-term urine retention is not identified in this case analysis.

Recent advances in minimal invasive surgery of pediatric urology

小兒泌尿微創手術的新進展

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The progress of many surgeries in the pediatric urology field had shifted from open surgery, standard laparoscopic, mini-laparoscopic, laparoendoscopic single-site incision (LESS), robotic-assisted pyeloplasty (RP) to robotic LESS surgery. Minimal invasive surgery had been introduced to pediatric fields for more three decades. Initially, the laparoscopy was only used as a diagnostic tool for undescended testis. With technical advances in smaller endoscopic instruments and high-resolution cameras, minimal invasive surgery became more widely accepted. Despite the promising advances in techniques and instruments in performing MIS, there were still many children received open surgeries in the past few years. The reasons may be due to steep learning curve-associated laparoscopic procedures. Robotic surgery was considered to be able to shorten the learning curve that was clearly shown in the adult surgery due to the outstanding stable magnified 3D view, tremor filtering, and motion scaling allow for precise intracorporeal exposure and suturing. Robot-assisted surgery was performed in pediatric pyeloplasty, radical and partial nephrectomy, ureteral reimplantation, kidney stones treatment, bladder augmentation, bladder neck reconstruction, Mitrofanoff appendicovesicostomy, and Malone antegrade continence enema. However, the training of technique in MIS become more and more difficult because of low birth rate in developed country. We urge the pediatric laparoendoscopists to improve the training program using new technology and the manufacturer to develop instruments directed for pediatric robotic-assisted surgery.

Prostate arterial embolization: Review of the literature and clinical practice experience

攝護腺動脈栓塞術：文獻回顧與臨床施作經驗分享

Chia-Bang Chen
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彰化基督教醫院 影像醫學部

Lower urinary tract symptoms (LUTS) has been an irritating problem to the elder people, and most of the LUTS are related to benign prostate hyperplasia (BPH). In the past the treatment modalities available for BPH includes the medications and surgical treatment, including transurethral resection of prostate (TURP), and in recent years greenlight laser prostatectomy and photo-selective vaporization (PVP) of the prostate has been emerging as promising options. However these surgical modalities carries some risk and may not be able to apply on people with multiple comorbidities.

Prostate arterial embolization (PAE) is a new and promising method to treat BPH-related LUTS. In experienced hands the prostatic arteries can be assessed using angiographic techniques, and embolization of these arteries leads to ischemic necrosis of the prostate parenchyma, and then decreased size of the prostate gland leads to relief of the LUTS. Compared with TURP, PAE is more tolerable and carries little procedure-related risk and complications, and shorter time of hospitalization is observed in the literature. About the treatment response, TURP and PAE both shows good result in the short-term follow-up within 1 year. However more patients in the PAE group have recurrent symptoms and may receive secondary treatment in the following years, either repeated PAE or TURP. As far there is no literature comparing greenlight laser prostatectomy or PVP to PAE.

In conclusion PAE is a good modality available to almost every patient who suffers from BPH-related LUTS, with less complications and shorter time of hospitalization, as compared with TURP. However the treatment effect may decrease in the long-term follow-up, and repeated treatment may be indicated.

A brief introduction of convective water vapour energy (WAVE) ablation for benign prostatic hyperplasia: The Rezum System

良性攝護腺肥大的水蒸氣消融治療：Rezum 系統

Wayne Lam

Division of Urology, Department of Surgery, Queen Mary Hospital, Hong Kong SAR

Benign prostatic hyperplasia (BPH) is extremely common, with a prevalence of almost 60% of men effected by the 7th decade of life in the Chinese population. Although with wellknown limitations such as bleeding, TUR syndrome, need of general or spinal anesthetics and post-operative hospital stay, transurethral resection of prostate is considered the 'reference standard' of surgical treatment of BPH when pharmacotherapy fails. To overcome the shortcomings of TURP, various minimally-invasive treatment for BPH have been developed recently. Rezum water vapour thermal therapy of the prostate appears to be one of the newest and very promising technique. Based on the unique convective water vapour energy (WAVE) principle, effective prostatic tissue destruction confined within the transition zone can be achieved under minimal anaesthesia, with the procedure feasible to be done as a day case. This lecture aims to review the latest evidence concerning Rezum, technique involved with the procedure, and to report our first-in-Asia initial experience in using Rezum in treating patients with BPH.

Laser operation for benign prostatic obstruction

良性攝護腺阻塞之雷射手術治療

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書田診所 泌尿科

Benign prostatic hyperplasia (BPH) is a histologic diagnosis that refers to the proliferation of the prostatic transition zone. Subsequent benign prostatic obstruction (BPO) developed while the enlargement obstructed the bladder neck. Parallel to these anatomical and functional processes, lower urinary tract symptoms (LUTS) increase in frequency and severity with age. The primary goal of surgical treatment has been to alleviate bothersome LUTS that result from BPO.

Traditionally, the obstructing adenomatous tissue was removed via open simple prostatectomy. Following the surgical plane, the enucleation of the hyperplastic prostatic adenoma is achieved with finger dissection. The transurethral resection of prostate using monopolar or bipolar electroconductivity has also been the treatment of choice. By finding the surgical capsule early in the procedure, the depth of the resection is set and followed thoroughly. Simple prostatectomy demonstrated durable improvement in voiding symptom score and superior peak urinary flow rate than TURP.

Nowadays, laser treatment of BPO has been an increasing choice for urologists and patients. Lasers are classified by their inherent wavelength and maximum output power. In statistics, lasers have favorable hemostatic properties that treat bleeding more effectively than monopolar energy in both laser enucleation group via Holmium laser(HoLEP) or Thulium laser(ThuLEP) and Photoselective Vaporization of the Prostate (PVP) group. Besides, the risk of dilutional hyponatreamia (TUR syndrome) has been eliminated with the use of isotonic, iso-osmolar irrigating solution in laser surgery.

Generally similar outcomes were reported regarding to symptomatic, urinary improvement in LUTS and complication rates between TURP and PVP. Laser enucleation represents the endoscopic response to open simple prostatectomy and is the most technically advanced laser prostate surgery. HoLEP and ThuLEP have similar outcomes when compared to TURP or simple prostatectomy as measured by I-PSS, I-PSS-QoL, Q_{max} outcomes, catheterization time, hospital stay, reoperation rate and post-surgical complication rate. Besides, laser enucleation is prostate size-independent suitable option for the treatment of LUTS attributed to BPO.

Although laser enucleation exhibits excellent results, a difficult and exaggerated learning curve has consistently been seen in adapters of this technique. The trend of laser operation is proceeding with surgeons' experience and encouraging treatment outcome.

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慢性傷口治療新進展

New Development of Chronic Wound Treatment

時　間：109年6月6日　13:30~17:30

Time：June 6, 2020　13:30~17:30

地　點：臺北榮民總醫院 科技大樓視訊會議室01013室

Place：Video Conference Room 01013
Medical Science and Technology Building
Taipei Veterans General Hospital

慢性傷口治療新進展

New Development of Chronic Wound Treatment

The importance of surgery in chronic wound care

手術治療在慢性傷口的重要性

Nguyen Anh Tuan

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Wound healing is a a complex biologic process, affected by many factors, especially chronic wounds. Wound treatment normally in general need to be combined many procedures, specialities with criteria: management a patient, not a wound.

Chronic wound, with characteristics: medical diseases (diabetes, blood vessel disease, stroke), infection, biofilm, hypoxia, poor nutrition, make it diffcult to heal and also make differences to acute wounds.

To treatment chronic wound normally we need meddle to local, area and system of body, in those: wound bed preparation, blood supply intervention, manage medical disease and surgery are the background of treatment.

Surgery in wound care can be blood vessel intervention, debridement, refresh wound, skin graft, flaps, etc. The advantages of surgery are: clean the wound, remove death tissue, foreign body, bring blood to the wound, fill up the defect, close the wound, etc.

In this talk, author will focus on the local surgical procedures those help to heal and/or close the wound as soon as possible. Some private experiences also will present.

The role of oxygen in wound healing

氧氣在傷口癒合的角色

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Topical oxygen therapy (TOT) approaches are not yet widely used in the wound care community anywhere in the world. While Growing evidence of its effectiveness suggests it has the potential to form a regular part of adjunctive therapies in treatment regimens to speed up healing of chronic wounds.

The benefits of using TOT for chronic wounds include improving angiogenesis, exert antimicrobial properties and enhance collagen production. Tissue hypoxia promotes angiogenesis via the activation of transcription factor HIF-1 (Hypoxia Inducible Factor 1), resulting in the upregulation of the vasculogenic cytokine such as VEGF (Vascular Endothelial Growth Factor), eventually leading to the migration and proliferation of endothelial cells and neovascularization. However, angiogenesis cannot be sustained in hypoxic environment.

Oxygen also has been shown to exert antimicrobial properties while promote wound healing. In addition, collagen production and maturation depends on oxygen. Central to the production of collagen lies in process hydroxylation which is carried out 2 respective hydroxylase of proline and lysine. The subsequent cross-linking of collagen which transform into its mature form is mediated is also oxygen-dependent. The latter step confers the added tensile strength required for extracellular environment. Wound hypoxia is associated with reduction of collagen production due to increase in the amount of MMPs and resultant delayed wound healing.

The developing new concept of therapeutic reconstructive ladder for chronic difficult wound: Experience in Tri-Service General Hospital

以三軍總醫院經驗談發展慢性困難傷口的治療重建階梯新觀念

Niann-Tzyy Dai
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Chronic wound, no matter how large the size, may comprise the characteristics of slow healing process more than 4 weeks, complicated underlying disorder such as poor controlled diabetes mellitus and peripheral arterial occlusive disease, lower limb venous stasis, or other systemic disorders. The standard therapeutic options may include advanced wound care, correction or stabilization of systemic diseases, debridement, and surgical reconstruction including skin graft, flap surgery or even amputation surgery. Up to date, newly therapeutic modalities emerged such as negative pressure wound therapy, continuous irrigation negative pressure wound therapy and cell therapy. In the contents of this topic, the newly developing therapeutic reconstructive concept for management of chronic difficult wounds will be proposed based on the clinical experience in Tri-Service General Hospital.

The chronic wounds presented here mainly include diabetic foot ulcer, peripheral arterial occlusive disease and necrotizing fasciitis. In the beginning, assessment of systemic disorders including blood sugar control, ABI, nutrition and anemia status and local wound condition including bacterial infection and 3-Dimentional wound size and depth will be launched. Next, correction and management of systemic problems should done including nutrition supplement, blood sugar control and reestablishment of peripheral circulations. Moreover, the standard wound care with multiple dressing modalities will be provided based on the Wound Watch Concept®. Finally, infection control, debridement of necrotic tissue and subsequent definite surgical therapeutic modalities will be conducted. However, in order to conquer the uncertainty of healing process of chronic difficult wounds, the new modalities may be intervened including negative pressure wound therapy, continuous irrigation negative pressure wound therapy and cell therapy. The experience of application of new medical devices and cell therapy in chronic difficult wound will be presented in this presentation.

Diagnosis and management of biofilm in complicated chronic wound

複雜慢性傷口上生物膜的診斷與治療

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鄭乃禎

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Complicated chronic non-healing wound has become a major worldwide healthcare burden. The impact of biofilms on chronic wound infection is well-established. The biofilm containing several types of bacteria exhibits higher resistance to the commonly-use antibiotics and the host immune responses. Despite increasing understanding of the underlying mechanism of biofilm formation in chronic wounds, current strategies for biofilm diagnosis and treatment in chronic wounds are still not ideal. Moreover, Therefore, novel technologies are required to fulfil this unmet clinical need, and the biofilm-based wound therapy therefore has been extensively stressed. Eradicating biofilms is critical for the effective treatment of chronic non-healing infected wounds, and a wide array of potential treatment options that are under development for biofilm removal in chronic wound infection. This procedure of biofilm-based wound care can be facilitated by timely and precise biofilm identification within the wound bed. Several reliable point-of-care diagnosis approach has emerged for detecting biofilms in chronic wounds. For instance, wound blotting-guided sharp debridement can lead to more accurate removal of biofilm-affected wound area without collateral damage to the neighboring granulation tissue. With the advent of new diagnostic tools, timely biofilm assessment may become readily available and biofilm-directed clinical treatment can be issued whenever necessary. The continuous development of sophisticated diagnostic and treatment approaches can markedly contribute to future implementation of biofilm eradication in chronic wound.

Smart telemedicine wound care project: Experience of NTUH Yunlin branch

智慧遠距傷口照護計畫：台大雲林分院經驗分享

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臺大醫院雲林分院 整形外科

World Health Organization has identified medical access, medical equality, quality of care and cost effectiveness as essential elements in developing health care. Advances in information and technology over the past decades provide great potentials in achieving these fundamental goals, especially among resource-scare areas. Supported by Ministry of Health and Warfare, we started the 'Yunlin Smart HealthCare Telemedicine Network Project' since 2018, and 'Smart telemedicine wound care project' is one of its subprojects. We aim to improve access and quality of care in a patient-centered model among a resource-scare area in Taiwan.

Through multi-institutional collaboration, we develop 'Smart telemedicine wound care project' in Yunlin County to evaluate the impact on access, quality of care and cost effectiveness. This project was implemented as three phases. During the first phase in 2018, we improved access of care for bed-ridden patients in nursing homes through remote wound assessment by plastic surgeons and onsite visits by wound-care specialists (nurses). Continuing the first phase, we expanded our services and improved our quality in the second phase in 2019. We included bed-ridden patients not only in nursing homes but also at home. We improved our quality of wound-care specialists by replacing nurses with nurse practitioners to perform standard wound care including maintenance debridement. In both phases, we applied smart wound care analysis device (inSight) for wound assessment. We are now in the third phase: combine onsite visits and remote monitoring.

Our complete wound healing rates are 42% (27 in 64 wounds) in phase one and 47% (145 in 310 wounds) in phase two.

Broaden the scope of wound care in the Digital Era: What could telemedicine and artificial intelligence bring change in wound care to us?

數位時代創新思維：人工智慧與視訊醫療在傷口照護帶來的新改變

Chih-Hsun Lin

林之勛

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臺北榮民總醫院 外科部 整形外科

Chronic wounds could severely compromise quality-of-life in the patients and always bring a challenge to the caregivers. The total cost of chronic wound care is a burden in medical economy and is getting higher as the aging society comes. Although there is advancement in the knowledge of wound healing, wound dressing, wound therapy and wound care, the pathways to delivery these technologies are still behind. Thus, our department try to incorporate the telemedicine and artificial intelligence to overcome the current dilemma in chronic wound care and try to improve care quality. The aim is to develop a model of integrated, effective and efficient wound care system.

First, Telemedicine 2.0 system is a concept of mobile medical service in wound care (teleACT). The system uses telecommunication technology to integrate nursing home care and hospital. Since Jan, 2019, we introduced teleACT model in evaluation of wound condition. The wounds were categorized into 1. Stable and 2. Requirement of transfer to hospital. For a population of 300 in nursing home care, we found the incidence of chronic wound is about 15.7% (n=47, 95% CI (Confidence Interval): 11.6-19.8%). Of these 47, the chronic wounds of 11 patients poorly progressed and required hospital assistance (n=11, 95% CI, 11.3-35.5%). 10 patients received the care of teleACT system between nursing home care and chronic wound center. One patient admitted through green pathway. Overall, these 11 patients had successful wound healing finally (wound healing rate 100%). The teleACT system could assist wound healing and reduce hospitalization.

Second, we developed an AI (Artificial Intelligence) program for assisting the diagnosis of wound condition. The AI was trained and the program verified by the wound photo database of our hospital. Under the training, the AI could establish its algorithm for wound evaluation. The major goal of the AI wound evaluation program is to assist non-professional medical personals, patients, and families for early warning of wound problems before the deterioration of wound condition. Other effects of AI wound evaluation reside on preventing late wound complications including sepsis, major limb amputation, and death. In addition, this AI system is expected to be integrated with teleACT model and our wound care center to provide a multi-dimensional and high-quality care of chronic wound.

Reconstruction for difficult chronic wound in the lower leg

小腿困難傷口重建

Mei-Chun Chen

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Reconstruction for lower leg is difficult due to limited soft tissue coverage and high risks of tendon and bone exposure. Patients with chronic lower limb wounds usually combined with chronic comorbidity, including diabetes mellitus, peripheral arterial occlusive disease, venous insufficiency, chronic wound infection or post-traumatic osteomyelitis. In acute trauma patients, the surgeon should evaluate the severity of limb injury, other associated organ injury and the possible functional outcome after limb amputation or limb preserving surgery. If limb preserving surgery is preferred, the wound may become a chronic wound due to extensive soft tissue loss or osteomyelitis. When preparing the good wound bed for the reconstruction, choosing suitable method of wound care according to different wound condition is important. We also need to control patient's underlying disease, evaluate the perfusion of the lower leg and debride the unhealthy tissue. The reconstruction methods for chronic wounds are including skin graft, local flap, free flap or amputation surgery. When the wound combines with diffuse skin defect with large area of tendon or bone exposure, amputation surgery may be considered. But disadvantage of amputation surgery are including independence threatened, difficult rehabilitation process, expensive prosthesis, phantom pain and the change in appearance. The advances of wound therapies and microsurgery help plastic surgeons preserve more limbs and improve patients' life quality. Free flap is widely used to provide soft tissue coverage with good perfusion to reconstruct extensive soft tissue loss in the lower limb. We will share the experience of reconstruction for difficult lower limb wounds in this topic.

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器官移植麻醉的回顧與展望

Review and Outlook of Anesthesia in Organ Transplantation

協辦單位：臺北榮民總醫院麻醉部
財團法人麻醉醫學研究發展基金會、臺灣麻醉醫學會

時　間：109年6月6日　　12:50~17:30
Time：June 6, 2020　　12:50~17:30

地　點：臺北榮民總醫院 科技大樓R01014討論室
Place：Discussion Room 01014
Medical Science and Technology Building
Taipei Veterans General Hospital

器官移植麻醉的回顧與展望

Review and Outlook of Anesthesia in Organ Transplantation

Anesthetic care for liver transplant in Taipei Veterans General Hospital, from goal-directed to individualized

臺北榮民總醫院肝臟移植麻醉照護經驗分享：從目標導向到個人化醫療

Shen-Chih Wang, Mei-Yung Tsou
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Debates remained in liver recipient perioperative care. We need to develop a strategic management to deal with complex and different surgical stages in liver transplant. The two major issues are hydration and transfusion. Overhydration leads to vein engorgement and increased blood loss. But underhydration results in kidney injury. Also, clinicians have to avoid unnecessary blood product use. In Taipei Veterans General Hospital, for perioperative liver recipients care, we used stroke volume variation derived from Flotrac to guide our hydration and thromboelastogram to guide our blood product use. To further improve our patient outcomes, we tend to explore new technologies utilization in patient managements. We have tried immune repertoire in differentiating infection and rejection. In spite of diversity, we apply manifold learning to extract more information from these sequencing data. We also try to analyze the arterial waveforms in anhepatic and neohepatic phases. With such extension of our clinical knowledge, we want to further tailor our perioperative managements for each individual patient toward a better outcome.

Sharing is caring: Our experience of pediatric liver transplant in Vietnam

醫療合作：我們在越南的小兒肝臟移植經驗

Mei-Yung Tsou, Shen-Chih Wang
鄒美勇 王審之
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Our transplant team, led by Professors Che-Chuan Loong and Chin-Su Liu, has been to Vietnam National Children Hospital for pediatric liver transplant for 8 times since 2007. Last year, nine cases, aged from 11 months to 16 years, were done collaborated with Vietnamese pediatric surgeons. With astonishing economic growth, Vietnam is a rising star in Southeast Asia. The birth rate in Vietnam is nearly twice to Taiwan. The age distribution of Vietnamese remains in expensive population pyramid and 23% of Vietnamese are under 15 years old. The demand of living donor liver transplant for pediatric patients is high in Vietnam. Taking the Vietnam National Children Hospital for example, nearly one hundred Kasai procedures were done last year. We hope to share our experience with these proficient Vietnamese pediatric surgeons and anesthesiologists and eventually they can finish the procedure independently.

Pancreas transplantation

胰臟移植

Yi-Ming Shyr, Shin-E Wang, Shih-Chin Chen, Bor-Uei Shyr
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Pancreas transplantation is currently the most effective and curative treatment for complicated type 1 diabetes mellitus (T1DM), providing durable and physiological insulin-independent euglycemia, preventing worsening or ameliorating of diabetic complications, and improving quality of life. Currently, more than 31,000 pancreas transplantation procedures have been performed, mainly in the United States. Pancreas transplantation is still an uncommon procedure in Asia, mainly performed in Korea, Taiwan and Japan. The first pancreas (simultaneous pancreas and kidney transplantation, SPK) transplantation was successfully initiated at Taipei Veterans General Hospital on September 19, 2003, and we are the first team to be qualified to perform human pancreas procurement and transplantation by Taiwan Department of Health on August 31, 2007. So far, we have performed 156 cases of pancreas transplantation at Taipei Veterans General Hospital. The technique success rate in our pancreas transplantation is 97%, with 1-year pancreas graft survival rate of 95.8%, 5-year pancreas graft survival rate of 89.9%, and 10-year pancreas graft survival rate of 65.9%.

Pain management after organ transplantation surgery

器官移植手術後的疼痛治療

Chun-Sung Sung

宋俊松

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Current clinical practices emphasize a multimodal and polypharmacy approach, with implementation of an enhanced recovery program and abidance by the guidelines on the management of postoperative pain from the APS, ASA and ASRA, to improve perioperative analgesia, reduce opioid use, and speed functional recovery after major surgery. Therefore, multimodal analgesia, including patient-controlled analgesia, central neuraxial and regional nerve block, fascial plan block, local surgical wound infiltration, the use of a variety of analgesics, and nonpharmacological interventions such as electric acupuncture and transcutaneous electric nerve stimulation, have been reported for the treatment of postoperative pain in both children and adult with good outcomes. Organ transplantation surgery may cause a high level of postoperative pain, as the surgery involves a long incision through either the chest or abdominal wall and organ harvest or implantation. Uncontrolled postoperative pain may lead to complications including increased morbidity and mortality, pulmonary and surgical site infection, ileus, delayed wound healing and mobilization, and longer hospital stays. Analgesia for organ transplantation surgery, both for recipient and living organ donor, has traditionally been managed with intravenous opioids; however, there are mounting reports of applying multimodal and opioid-sparing polypharmacy in this population. It should be taken into organizing the post-transplant pain management plan in patients without contraindications.

The anesthesia experience and future of heart transplantation

心臟移植麻醉的經驗與未來發展

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Heart transplantation has become a standard treatment for selected patients with end-stage heart failure. Improvements in immunosuppressants, surgical techniques, perioperative support, and post-transplant care have gained a substantial increase of survival. Meticulous anesthesia management is essential for induction in these advanced heart failure patients and cardiovascular recovery after donor heart transplant.

In Taiwan, mechanical cardiac support, including intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), or left ventricular assist device (LVAD), is getting more popular for bridge-to-transplantation in recent years. Anesthesia with heart failure symptoms and monitoring for common VAD-related complications ensure viability of heart transplant candidates. As expected, we'll encounter a growing number of left LVAD patients undergoing noncardiac surgery.

Anesthesia for lung transplantation: Twenty-year experience at NTUH

肺臟移植麻醉：台大經驗分享

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Lung transplantation has been performed in National Taiwan University Hospital since 1995. It is a complicated surgery that takes a lot of manpower and time. The postoperative care of patients is quite hard, too. In the face of patients with variable diagnosis and cardiopulmonary conditions, the anesthesia management and intraoperative monitoring are complicated. Close cooperation with surgeons and extracorporeal membrane oxygenation (ECMO) team is also important. Under the call of the late professor of thoracic surgery, Yung-Chie Lee, our hospital set up a cross-disciplinary lung transplant team. Headed by Professor Hsao-Hsun Hsu, we have completed more than 100 lung transplants which is more than half of the cases in Taiwan.

Different managements such as single-lung ventilation, cardiopulmonary bypass, or ECMO support are required during anesthesia for lung transplantation. Hemodynamics during different operation stages, especially during lung reperfusion, must be carefully controlled to protect the fragile transplanted lungs. In addition to the traditional monitoring, transesophageal echocardiography can be used not only to assess the hemodynamic status immediately but also to evaluate the condition of vascular anastomosis. Moreover, the inter-departmental cooperation is emphasized for postoperative pain management.

Although limited by the number of donations, lung transplantation in our hospital has achieved a stable performance after a long-time effort. In recent years, the prognosis of our patients has been better than the average of the world. Bilateral sequential single lung transplantation under ECMO support is the main operation method. The use of ECMO reduces the instability during operation and postoperative care. In addition to the easier control of oxygenation and hemodynamics, the blood loss during operation is much lower than those under cardiopulmonary bypass. It also reduces the risk of primary graft dysfunction which is related to the amount of transfusion. Last year, we shared our experiences and helped the team of Vietnam to perform lung transplantation successfully by themselves.

With the progress in organ preservation and operation techniques, the survival rate of lung transplantation is gradually increased in the world. However, the prognosis of it is still the worse in all organ transplantations. We hope that the efforts of us can finally help the struggled patients to survive.

Experience of anesthesia for small bowel transplantation

小腸移植麻醉經驗分享

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Small bowel transplantation is the therapy for irreversible intestinal failure. Common causes of intestinal failure include short-gut syndrome, motility or absorptive disorder, and neoplasm. These patients usually depend on total parenteral nutrition (TPN) to sustain their life. However, when patients encounter TPN-related complications, such as impending liver failure, lack of central vein access, frequent line infection or sepsis, or episodes of dehydration, small bowel transplantation is indicated.

Before anesthesia, we should evaluate the patient about the cause of intestinal failure, previous operation history, patient's cardiac condition (ECG, echocardiography), conditions of central vein (Doppler ultrasonography, contrast venography, MRA), and any other comorbidities. Besides of arterial line and central venous line, anesthesia preparation may include continuous cardiac output monitoring, TEE, and BIS. Rapid sequence induction should be considered if patients suffer from delayed gastric emptying.

The surgery can be divided into three phases: the dissection phase, the vascular anastomoses phase, and after reperfusion, the intestinal reconstruction phase. Significant blood loss may be anticipated during the dissection and anastomoses phase. After reperfusion, changes in vascular tone and intravascular fluid shift may result in significant drop in blood pressure, which can be managed with fluid replacement (particularly colloid) and vasoactive agent. Special attention should also be paid to potassium level and body temperature after reperfusion.

Graft rejection is still the main cause of graft failure after transplantation. Future improvement in immunosuppression may prolong graft and patients' survival. On the other hand, pharmacologically enhancing intestinal adaptation and autologous gastrointestinal reconstruction may reduce the necessity of intestinal transplantation.

「醫學研究論文獎」及
「盧致德獎」論文摘要

「盧致德獎」
(從刊登於中華醫學會雜誌上的全部論文中，選出被引用
20 次以上的作者，並以其中最多次者頒發盧致德獎)

「醫學研究論文獎」及「盧致德獎」論文摘要

1 財團法人中華醫學研究獎助基金會
Does continued aspirin mono-therapy lead to a higher bleeding risk after total knee arthroplasty? ..... 臺北榮總 骨科部 陳正豐醫師

2 財團法人消化醫學研究發展基金會
Antiviral effect of saikosaponin B2 in combination with daclatasvir on NS5A resistance-associated substitutions of hepatitis C virus ..... 臺北榮總 醫研部 李偉平醫師

3 財團法人兼善醫學基金會
Clusterin expression in nontumor tissue in patients with resectable hepatocellular carcinoma related with postresectional survival ..... 臺北榮總 一般外科 郭栢仲醫師

4 財團法人心臟醫學研究發展基金會
Combined surgical and endovascular treatment with arch preservation of acute DeBakey type I aortic dissection ..... 臺北榮總 心臟外科 許喬博醫師

5 財團法人泌尿外科醫學研究發展基金會
Risk factors for hypogonadism in young men with erectile dysfunction ..... 臺北榮總 泌尿部 黃奕燊醫師

6 財團法人思源內科醫學研究發展基金會
Effect of ivabradine, a funny current inhibitor, on portal hypertensive rats ..... 臺北榮總 一般內科 張景智醫師

7 財團法人吳舜文神經科學發展基金會
Development and validation of a Taiwan version of the DN4-T questionnaire ..... 臺北榮總 神經內科 王嚴鋒醫師

8 財團法人台灣癌症臨床研究發展基金會
Gene amplification and tumor grading in parosteal osteosarcoma ..... 臺北榮總 一般病理科 陳志學醫師

9 財團法人中華醫學研究獎助基金會
Intermediate Syndrome Following Organophosphate Insecticide Poisoning ..... 臺北榮總 臨床毒物與職業醫學科 楊振昌醫師

Journal of the Chinese Medical Association (2019) 82: 60-65

Does continued aspirin mono-therapy lead to a higher bleeding risk after total knee arthroplasty?

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Abstract

Background. Evidence about the risk of bleeding and thromboembolism because of aspirin mono-therapy in total knee arthroplasty (TKA) is scant. We wanted to validate the risks of bleeding and thromboembolism with continued aspirin mono-therapy in unilateral and simultaneous bilateral TKA.

Methods. We enrolled a series of 1655 patients who underwent unilateral or simultaneous bilateral TKA between December 2010 and December 2012. Drainage amount, postoperative hemoglobin level, change in hemoglobin, calculated blood loss, incidence and the amount of blood transfused, and the proportion of thromboembolic events were compared between patients who were and patients who were not on continued aspirin mono-therapy.

Results. Calculated blood loss (969.1 ± 324.9 vs. 904.0 ± 315.5 ml), transfusion amounts (1.3 ± 1.5 vs. 1.0 ± 1.3 IU), and percentage of transfused patients (53.0% vs. 40.2%) were higher in unilateral TKA patients on continued aspirin mono-therapy. Outcome parameters and the proportion of DVT between groups were not significantly different. One patient (0.3%) not on aspirin mono-therapy developed a pulmonary embolism, and two others (0.6%) had cerebrovascular events.

Conclusion. Despite the slightly higher risks of bleeding, continuing aspirin mono-therapy during TKA might be safe with low risks of perioperative cerebrovascular, cardiovascular, and venous thromboembolic events.

Keywords. Aspirin; Bleeding risk; Monotherapy; Thromboembolism; Total knee arthroplasty

Journal of the Chinese Medical Association (2019) 82: 368-374

Antiviral effect of saikosaponin B2 in combination with daclatasvir on NS5A resistance-associated substitutions of hepatitis C virus

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Abstract

Background. Hepatitis C virus (HCV) is a major causative agent of chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The rapid progress in the development of direct-acting antivirals[1] has greatly elevated the cure rate to ≥95% in recent years. However, the high cost of treatment is not affordable to patients in some countries, necessitating the development of less expen- sive treatment.

Methods. We adopted a cell culture-derived HCV system to screen a library of the pure compounds extracted from herbs deposited in the chemical bank of the National Research Institute of Chinese Medicine, Taiwan.

Results. We found that saikosaponin B2 inhibited viral entry, replication, and translation. Saikosaponin B2 is a plant glycoside and a component of *x*iao-chai-hu-tang, a traditional Chinese herbal medicine extracted from the roots of *Bupleurum falcatum*. It also inhibited daclatasvir-resistant mutant strains of HCV, especially in combination with daclatasvir.

Conclusion. Our results may aid the development of a new combination therapy useful for patients with HCV who are intolerant or refractory to the currently available medications, including pegylated interferon and direct-acting antiviral agents.

Keywords. Daclatasvir; HCV; NS5A; Resistance-associated substitution; Saikosaponin

Journal of the Chinese Medical Association (2019) 82: 929-934

Clusterin expression in nontumor tissue in patients with resectable hepatocellular carcinoma related with postresectional survival

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Abstract

Background. Surgical resection offers an effective treatment for patients with hepatocellular carcinoma (HCC); however, it has high tumor recurrence rate. Clusterin is a highly conserved glycoprotein that enhances cell aggregation in vitro. It is upregulated in several types of cancers such as breast, ovarian, colon, prostate and kidney cancers, and HCC. Clusterin overexpression is correlated with tumor metastasis. We evaluated the significance of clusterin expression levels in serum and resected tissues of patients with HCC.

Methods. Serum, resected tumor tissue, and nontumor tissue were collected from 140 patients with HCC undergoing hepatic resection. Serum clusterin levels were determined by enzyme-linked immunosorbent assay. Clusterin expression in resected tissue was evaluated by immunohistochemistry. Median follow-up time was 57.8 months.

Results. Mean serum clusterin levels were found to be 130.0 ± 58.7 μg/mL (range, 10.1-366.6 μg/mL). Serum clusterin levels were independent of tumor stage and deterioration of liver function in patients. No significant difference was observed in the survival of patients with high (>130.0 ± 58.7 μg/mL) or low (≤130.0 ± 58.7 μg/mL) serum clusterin level. Clusterin was expressed in HCC tissues of 76 patients (54.3%) and nontumor liver tissues of 53 patients (37.9%). No significant difference was observed in the survival of patients with positive or negative clusterin expression in HCC tissues. In nontumor tissues, patients with positive clusterin expression were observed to have low postoperative disease-free survival rate (p = 0.001) compared to patients with negative clusterin expression. Multivariate analysis showed that tumor with macrovascular/microvascular invasion and clusterin expression in nontumor tissues are independent prognostic factors following hepatic resection.

Conclusion. In HCC, clusterin expression in nontumor tissue shows worse prognosis after hepatic resection. Clusterin can be a prognostic marker for patients with postresection HCC.

Keywords. Clusterin; Hepatocellular carcinoma; Outcome predictor

Journal of the Chinese Medical Association (2019) 82: 209-241

Combined surgical and endovascular treatment with arch preservation of acute DeBakey type I aortic dissection

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Abstract

Background. DeBakey type I aortic dissection is a catastrophic event that presents a formidable challenge to cardiovascular surgeon. Here, we evaluate a new combined surgical and endovascular technique for acute condition.

Methods. Between December 2011 and December 2015, 12 patients with type I aortic dissection concomitant involving supra-aortic vessels underwent ascending aortic replacement and simultaneous stent grafts inserted into the descending aorta, left subclavian, and left carotid arteries, and into the innominate artery when possible, without arch replacement. The stent grafts, Gore TAG thoracic endoprosthesis and Viabahn, were deployed under visual guidance through opened aortic arch into the true lumen, with the techniques of circulatory arrest, moderate hypothermia, and bilateral antegrade cerebral perfusion.

Results. Operation was performed smoothly in all patients. There was one death, and the other 11 recovered without any neurological deficits. Follow-up computed tomography scans showed that the true lumen expanded and false lumen regressed in both arch and descending aortic segments in 1 year. The diameter did not increase in either arch or descending aortic segments.

Conclusion. Ascending aortic replacement and stent graft for supra-aortic arteries and the descending aorta without arch replacement are feasible options for type I aortic dissection with satisfactory short-term aortic remodeling.

Keywords. Aortic dissection; Hypothermia; Descending aorta

Journal of the Chinese Medical Association (2019) 82: 477-481

Risk factors for hypogonadism in young men with erectile dysfunction

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Abstract

Background. The objective of this study is to evaluate the hormone profile of young men with the chief complaint of erectile dysfunction (ED) and determine the comorbidities in this population.

Methods. A retrospective chart review of men aged 18 to 40 years who presented with ED and had a hormone evaluation but without prior medication for hormone manipulation from 2002 to 2016 was performed at a tertiary care institution. Data were obtained on demographics, comorbidities, medications, and hormonal evaluations.

Results. A total of 2292 men with ED were identified and 2130 of them received testosterone level evaluation. The most common comorbidities that men were actively being treated for were depression (22.3%), anxiety (16.1%), hypertension (15.6%), diabetes (7.2%), cancer (6.2%), and cardiovascular disease (3.3%). The average total testosterone level was 368 ± 160 ng/dL; 10.7% of men had hypogonadism. Multivariate analysis demonstrated age, body mass index (BMI), depression, and cancer predicted a hypogonadal status. Patients with BMI > 28.2 kg/m^2, age > 34 years, cancer diagnosis, or depression were 3.350-fold, 1.447-fold, 2.317-fold, or 1.420-fold more likely to be diagnosed hypogonadal than nonoverweight, age ≤ 34 years, noncancer, or nondepressive patients.

Conclusion. The majority of men under the age of 40 with ED exhibit a normal hormonal milieu. Young ED men with BMI > 28.2 kg/m^2, age >34 years, cancer diagnosis, or depression are at risk for hypogonadism.

Keywords. Erectile dysfunction; Hormone; Hypogonadism; Men

Journal of the Chinese Medical Association (2019) 82: 19-24

Effect of ivabradine, a funny current inhibitor, on portal hypertensive rats

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Abstract

Background. Ivabradine is a funny current inhibitor which is administered to patients with congestive heart failure to reduce their heart rate (HR) and attenuate oxidative stress. Chronic liver diseases are characterized by portal hypertension and hyperdynamic circulation with tachycardia. The present study aimed to investigate the effect of ivabradine on portal hypertension.

Methods. MaleSprague–Dawley rats received partial portal vein ligation (PVL) to induce portal hypertension. The PVL ratswere randomly allocated to receive either vehicle or ivabradine treatment for 10 days. Then the hemodynamic datawere collected. The levels of oxidative stressmarkers and the mRNA expression of nitric oxide synthase (NOS) were measured in the collateral vessel, the superior mesentery artery and the liver. In addition, the collateral vascular responsiveness to arginine vasopressin (AVP) was examined in the ivabradine-treated and vehicle-treated PVL rats.

Results. Treatment with ivabradine significantly lowered the HR (174 ± 20 vs. 374 ± 9 beats/min; $p < 0.001$) and the superior mesentery arterial flow (SMAf) (6.6 ± 0.3 vs. 9.1 ± 0.7 mL/min/100 g BW; $p = 0.005$) of the PVL rats compared with the control group. The mean arterial pressure, cardiac index, systemic vascular resistance, portal pressure and serum levels of oxidative stress markers were not significantly affected by ivabradine treatment. In addition, the NOS expression and collateral vascular responsiveness to AVP were not significantly influenced by ivabradine treatment, either.

Conclusion. Ivabradine reduced the HR and SMAf in PVL rats, which alleviated the hyperdynamic circulatory state and splanchnic hyperemia of portal hypertension. However, whether these effects would help alleviate portal hypertension-related complications requires further clinical investigations.

Keywords. Heart rate; Hyperdynamic circulation; Ivabradine; Nitric oxide; Portal hypertension

Journal of the Chinese Medical Association (2019) 82: 623-627

Development and validation of a Taiwan version of the DN4-T questionnaire

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Abstract

Background. Neuropathic pain (NeP) is often under-recognized, resulting in poor pain management. Therefore, a Taiwan version of the 10-item Douleur Neuropathique 4 (DN4-T) questionnaire was developed to identify patients with NeP from a mixed population of patients with pain.

Methods. A prospective, nonrandomized, multicenter study was conducted in the Neurology Departments of four Taiwanese medical centers, to develop and validate the DN4-T questionnaire as a diagnostic tool for identifying patients with NeP. Patients who experienced pain for >30 days were classified as having neuropathic, nociceptive, or mixed pain. Patients and physicians also completed the DN4-T questionnaire. The DN4-T scores were assessed with the optimal cut-off score calculated using a receiver operating characteristics (ROC) curve, and sensitivity and specificity assessed and reliability determined statistically using the Cronbach alpha coefficient.

Results. Of the 318 patients who completed the DN4-T questionnaire, 189 patients were diagnosed with NeP, seven patients with mixed pain, and 122 patients with nociceptive pain. For statistical analysis, patients were categorized as having NeP (those with neuropathic pain and mixed pain) or non-neuropathic (nociceptive) pain (non-NeP). Using an optimum DN4-T cut-off score of ≥3 (ranging from 0 to 10, determined by a maximum c index value of 1.54), DN4-T scores provided a sensitivity of 0.77 and specificity of 0.78, for predicting NeP. The predictive power of DN4-T in diagnosing NeP was 0.83 (as determined by area under the curve of the ROC curve), and was significantly predictive of pain type ($p < 0.0001$) with a concordance of 0.785, a discordance of 0.129, and a Cronbach alpha coefficient of 0.7, suggesting that the DN4-T questionnaire is a useful predictive tool for diagnosing NeP.

Conclusion. The DN4-T questionnaire has been reliably translated into Mandarin Chinese and can be used as a diagnostic tool for NeP in conjunction with clinical evaluation.

Keywords. DN4; Neuropathic pain; Questionnaire; Taiwan

Journal of the Chinese Medical Association (2019) 82: 889-894

Gene amplification and tumor grading in parosteal osteosarcoma

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Abstract

Background. Parosteal osteosarcoma (POS) is a unique low grade osteosarcoma. Two separate oncogenes, *MDM2* and *CDK4*, are specifically amplified in POS. Its clinical behavior is usually indolent. In some occasions, it may progress to high grade and become fatal. Malignant transformation with high grade differentiation is the most reliable indicator to predict its aggressiveness and metastatic potential. This study is to discover the relationship between gene amplification and grading.

Methods. Retrospective analysis of MDM2/CDK4 expression/amplification using immunostaining, multiplex quantitative polymerase chain reaction (MQPCR) and fluorescence *in situ* hybridization (FISH) were studied on 14 patients with recurrent POS.

Results. Forty tumor specimens in formalin-fixed paraffin-embedded blocks from 14 patients of POS were included in this study. Twenty-seven tumors are low-grade, 13 are high-grade. All POS showed increased expression of both MDM2 and CDK4 proteins, but not those from conventional osteosarcoma. Except some tumors were non-informative (poor DNA quality), the rest of POS had a marked increase of *MDM2* and *CDK4* genes copies by MQPCR, and confirmed by *MDM2* FISH. Moreover, the folds of amplification increase as tumors progress. And, the amplification folds in high-grade POS are consistently higher than those of conventional ones.

Conclusion. FISH and MQPCR are both useful assays for estimating oncogene amplification status in bone tumors. Amplification levels of *MDM2* and *CDK4* are related to tumor grading and progression. Molecular determination of gene amplification status can be a reliable alternative for predicting clinical behavior of POS at small biopsies.

Keywords. Amplification; Dedifferentiation; Parosteal osteosarcoma

Journal of the Chinese Medical Association (2007) 70: 467-472

Intermediate Syndrome Following Organophosphate Insecticide Poisoning

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Abstract

Acute organophosphate insecticide poisoning can manifest 3 different phases of toxic effects, namely, acute cholinergic crisis, intermediate syndrome (IMS), and delayed neuropathy. Among them, IMS has been considered as a major contributing factor of organophosphate-related morbidity and mortality because of its frequent occurrence and probable consequence of respiratory failure. Despite a high incidence, the pathophysiology that underlies IMS remains unclear. Previously proposed mechanisms of IMS include different susceptibility of various cholinergic receptors, muscle necrosis, prolonged acetylcholinesterase inhibition, inadequate oxime therapy, downregulation or desensitization of postsynaptic acetylcholine receptors, failure of postsynaptic acetylcholine release, and oxidative stress-related myopathy. The clinical manifestations of IMS typically occur within 24 to 96 hours, affecting conscious patients without cholinergic signs, and involve the muscles of respiration, proximal limb muscles, neck flexors, and muscles innervated by motor cranial nerves. With appropriate therapy that commonly includes artificial respiration, complete recovery develops 5–18 days later. Patients with atypical manifestations of IMS, especially a relapse or a continuum of acute cholinergic crisis, however, were frequently reported in clinical studies of IMS. The treatment of IMS is mainly supportive. Nevertheless, because IMS generally concurs with severe organophosphate toxicity and persistent inhibition of acetylcholinesterase, early aggressive decontamination, appropriate antidotal therapy, and prompt institution of ventilatory support should be helpful in ameliorating the magnitude and/or the incidence of IMS. Although IMS is well recognized as a disorder of neuromuscular junctions, its exact etiology, incidence, and risk factors are not clearly defined because existing studies are largely small-scale case series and do not employ a consistent and rigorous definition of IMS. Without a clear understanding of the pathophysiology of IMS, specific therapy is not available. The prognosis of IMS, however, is likely to be favorable if respiratory failure can be promptly recognized and treated accordingly. [*J Chin Med Assoc* 2007;70(11):467–472]

Key Words. acetylcholine, cholinergic crisis, intermediate syndrome, organophosphate insecticide poisoning

銘謝贊助單位

臺北榮民總醫院、臺中榮民總醫院、高雄榮民總醫院

科技部

財團法人鄒濟勳醫學研究發展基金會

公益信託林堉璘宏泰教育文化公益基金

財團法人林堉璘宏泰教育基金會

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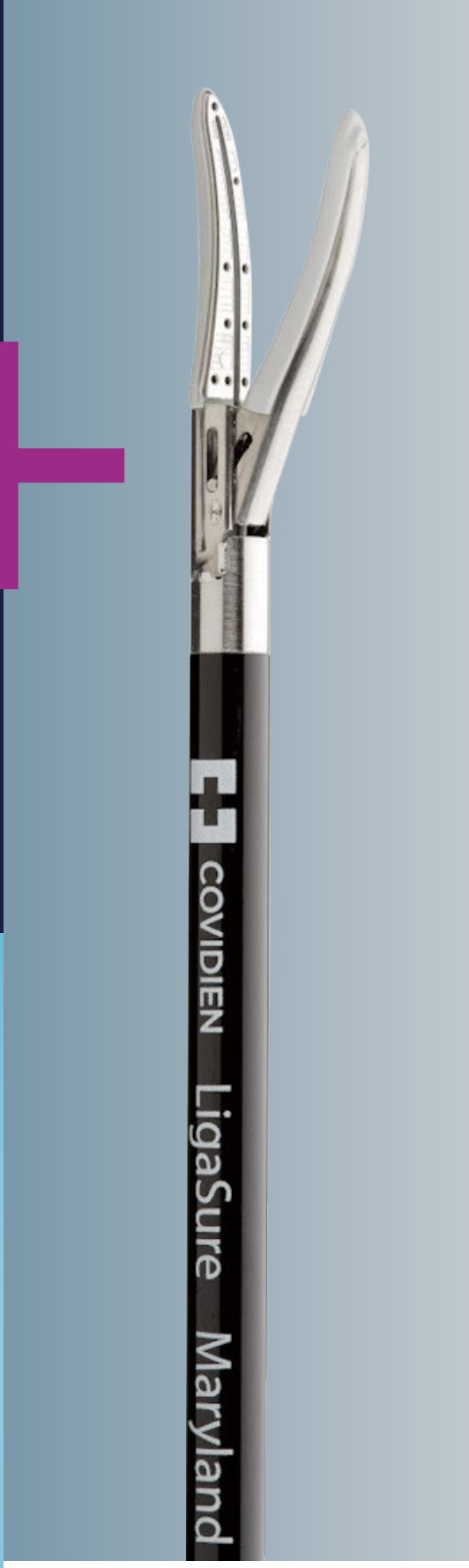

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- 含有 Human Fibrinogen 及 Human Thrombin，模仿人體凝血機轉
- Synthetic Aprotinin 作為抗纖維蛋白溶解劑，預防纖維蛋白凝塊過早分解

Reference :

1. Sierra DH. Fibrin sealant adhesive systems: a review of their chemistry, material properties and clinical applications. *J. Biomater Appl.*

BioSurgery | ADVANCING SURGERY, ENHANCING LIFE

Baxter

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使用前請詳閱說明書警語及注意事項

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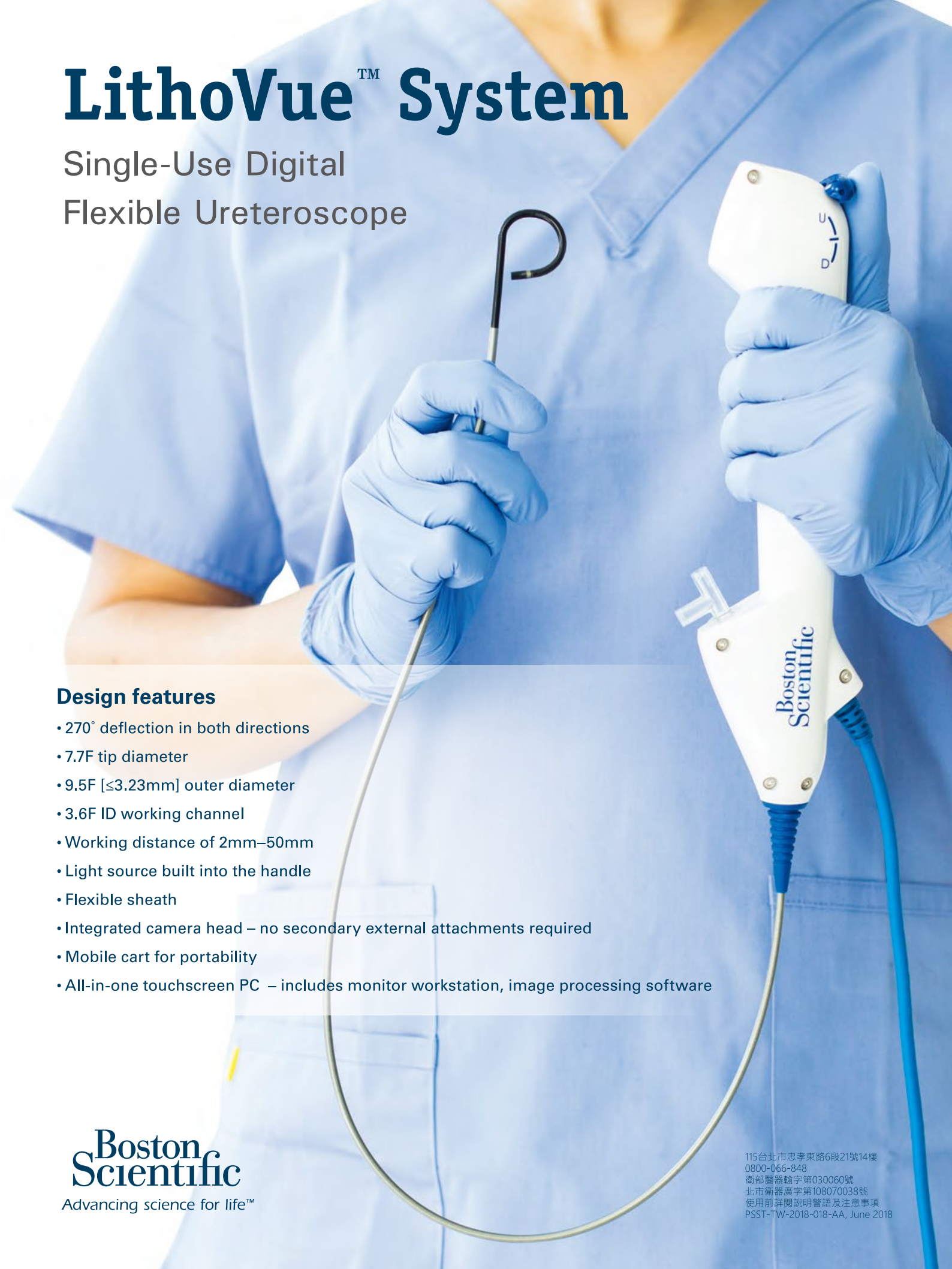
LithoVue™ System

Single-Use Digital Flexible Ureteroscope



Design features

- 270° deflection in both directions
- 7.7F tip diameter
- 9.5F [≤3.23mm] outer diameter
- 3.6F ID working channel
- Working distance of 2mm–50mm
- Light source built into the handle
- Flexible sheath
- Integrated camera head – no secondary external attachments required
- Mobile cart for portability
- All-in-one touchscreen PC – includes monitor workstation, image processing software

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使用前詳閱說明警語及注意事項
PSST-TW-2018-018-AA, June 2018