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PADCEV
enfortumab vedotin

Efficacy

PADCEV合併Pembrolizumab用於一線 Cisplatin-Ineligible LA/mUC 療法ORR達68%[4,5,7]

Reimbursement

PADCEV健保給付於先前接受過含鉑化療 和免疫檢查點PD-1、PD-L1抑制劑之LA/mUC治療[2,6]

All-comer

Nectin-4 高度表現於泌尿上皮癌， 使用 PADCEV 前無須基因檢測 [3]

PADCEV 適應症：

1. 單獨使用適用於治療患有局部晚期或轉移性泌尿道上皮癌的成人病人：
   (1) 先前接受過PD-1（programmed death receptor-1）或 PD-L1（programmed death-ligand 1）抑制劑和含鉑化學治療；或
   (2) 不適合接受含cisplatin化學治療，且先前接受過一線以上治療。
2. 併用 pembrolizumab 適用於治療不適合接受含cisplatin化學治療的局部晚期或轉移性泌尿道上皮癌的成人病人。

此適應症係依據腫瘤整體反應率及反應持續時間加速核准，此適應症仍須執行確認性試驗以證明其臨床效益。

【禁忌】
無。
【警語及注意事項】
特殊警語：嚴重皮膚不良反應
PADCEV可能會引起嚴重且致命的皮膚不良反應，包括史蒂文生—強生症候群（Stevens-Johnson syndrome，SJS）和毒性表皮壞死溶解症（Toxic Epidermal Necrolysis，TEN）；主要發生在第一個治療週期，但也可能在之後發生。
密切監測病人的皮膚反應。
當疑似SJS、TEN、或嚴重皮膚反應，立即停止給予PADCEV，並考慮將病人轉介給專科照護。
對確診SJS或TEN、或發生4級或復發性3級皮膚反應的病人，永久停用PADCEV。
【不良反應】
臨床重要副作用/不良反應
嚴重不良反應：皮膚反應、高血糖症、肺炎 (pneumonitis) /間質性肺病（ILD）、周邊神經病變、眼部疾患、輸注部位外滲

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1. EV201 Cohort 2.Lancet Oncol 2021 Jun;22(6):872-882 2.EV301, N Engl J Med 2021 Mar 25;384(12):1125-1135 3.EV101,J Clin Oncol 38:1041-1049. 4.台灣仿單
5.EV-103 Cohort K, J Clin Oncol. 2023 Sep 1;41(25):4107-4117 5.EV-103 Cohort K, J Clin Oncol. 2023 Sep 1;41(25):4107-4117 6.全民健康保險藥物給付項目及支付標準第9節抗癌瘤藥物
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暨聯合學術研討會

1

精準醫療於遺傳性疾病

Precision Medicine in Genetic Disease

時　間：113年6月22日　08:30-17:30

Time：June 22, 2024　08:30-17:30

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

精準醫療於遺傳性疾病
Precision Medicine in Genetic Disease

Gene therapy for Fabry disease

法布瑞氏症的基因治療

Michael West

Division of Nephrology, Department of Medicine, Dalhousie University & Nova Scotia Health, Canada

加拿大達爾豪斯大學 醫學系 腎臟科

Gene therapy is the delivery of a therapeutic gene for endogenous cellular expression with the goal of rescuing a disease phenotype. It has been used to treat an increasing number of human diseases with many strategies proving safe and efficacious in clinical trials. Gene delivery may be viral or non-viral, performed in vivo or ex vivo, and relies on gene integration or transient expression; all of these techniques have been applied to the treatment of Fabry disease.

Fabry disease is a genetic disorder of the α-galactosidase A gene, *GLA*, that causes an accumulation of glycosphingolipids in cells leading to cardiac, renal and cerebrovascular damage and eventually death. Currently, there are no curative treatments available, and the therapies that are used have significant drawbacks. These treatment concerns have led to the advent of gene therapies for Fabry disease. The first Fabry patients to receive gene therapy were treated with recombinant lentivirus targeting their hematopoietic stem/progenitor cells. Adeno-associated virus treatments have also begun. Alternatively, the field of gene-editing is a new and rapidly growing field. Gene-editing has been used to repair disease-causing mutations or insert genes into cellular DNA. These techniques have the potential to be applied to the treatment of Fabry disease provided the concerns of gene-editing technology, such as safety and efficiency, were addressed. This talk will discuss the current state of gene therapy as it is being developed for Fabry disease, including progresses and challenges as well as an overview of gene-editing and how it may be applied to correct Fabry disease-causing mutations in the future.

Prevention and treatment of complications in gene therapy

基因治療併發症的預防與治療

Hsin-Hui Wang

王馨慧

Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Department of Pediatrics, School of Medicine, College of Medicine, and Institute of Emergency and Critical Care Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 兒童醫學部 兒童免疫腎臟科

國立陽明交通大學 醫學院 醫學系 小兒學科暨急重症醫學研究所

Gene therapy has great potential to treat genetic diseases, but it also faces significant challenges that require careful management to ensure patient safety and therapeutic efficacy. It is critical to address complications such as safety risks, genotoxicity, immunogenicity, and toxicity.

Efforts are ongoing to develop safer vehicles and to personalize delivery routes based on individual characteristics. Strategies to modulate immunity play a key role in minimizing immunogenicity-related problems, while controlling complications through symptom control, dose adjustment, or targeted therapy requires immediate intervention.

Although site-specific gene editing approaches can reduce risks, genotoxicity remains a concern, especially for viral vectors. Despite advances, gene-editing technologies still carry inherent genotoxic risks. Immunogenicity poses challenges, particularly with AAV-based therapies, where pre-existing immunity may hinder efficacy. Therefore, strategies to overcome immune responses are imperative. Toxicity, including hepatotoxicity and thrombotic microangiopathy (TMA), requires vigilant monitoring and management. Optimizing vector design, dosing regimen, and immune modulation are key strategies to prevent and mitigate toxicity. Approaches to mitigate immunogenicity include vector engineering, immunomodulatory drugs, plasma exchange, and enzyme-based antibody cleavage.

Overall, successful gene therapy requires a multidisciplinary approach and ongoing research to optimize vector components, dosing regimens, and immunomodulatory strategies. Long-term monitoring and careful management of complications are critical to realizing the full potential of gene therapy and improving patient outcomes.

Pegunigalsidase alfa: A novel, pegylated recombinant alpha-galactosidase enzyme for the treatment of Fabry disease

Pegunigalsidase alfa：一種新型的聚乙二醇化重組 α- 半乳糖苷酶，用於治療法布瑞氏症

Dominique P. Germain

Division of Medical Genetics, University of Versailles, France

Distinguished Center Scientist, Veteran General Hospital, Taipei, Taiwan, ROC

法國凡爾賽大學 醫學遺傳學系

臺北榮民總醫院 遺傳諮詢中心傑出科學家

Fabry disease a rare X-linked genetic disorder, results from pathogenic variants in the *GLA* gene, leading to deficient lysosomal α-galactosidase A enzyme activity and multi-organ manifestations. Since 2001, enzyme replacement therapy (ERT), using agalsidase alfa or beta, has been the mainstay treatment, albeit with limitations such as rapid clearance and immunogenicity. Pegunigalsidase alfa, a novel PEGylated recombinant alpha-galactosidase, offers promise as an alternative. Produced in plant cells, pegunigalsidase alfa exhibits enhanced stability, prolonged half-life, and reduced immunogenicity due to pegylation. A phase 1/2 clinical trial followed by an extension study up to 60 months showed Gb3 clearance from renal capillary endothelial cells and notable outcomes in renal function preservation. Three phase 3 clinical trials (BRIDGE, BRIGHT, and BALANCE) have shown favorable efficacy and safety profile, particularly in patients with deteriorating renal function, although caution is warranted in interpreting the results of the BRIDGE and BRIGHT studies which lacked control groups. The BALANCE study, a pivotal phase 3 trial comparing pegunigalsidase alfa with agalsidase beta, revealed in an intention-to-treat analysis of the eGFR decline over 2 years, that the intergroup difference [95%CI] in the median slope was -0.36 mL/min/1.73 m2/year [-2.44; 1.73]. The confidence interval had a lower limit above the prespecified value of -3 mL/min/1.73 m2/year and included zero (indicating that the intergroup difference was not significant). Despite challenges such as IgE-mediated hypersensitivity reactions and immune-complex-mediated glomerulonephritis, pegunigalsidase alfa's approval by the European Medicines Agency and Food and Drug Administration represents a significant addition to Fabry disease therapeutic landscape providing an option for patients in whom the *GLA* variant is not amenable to chaperone therapy or ERT with agalsidase alfa or agalsidase is poorly tolerated or poorly effective.

Early detection of irreversible cellular damage in cardiac biopsies of Fabry disease before the Formation of Gb3 inclusion bodies

法布瑞氏症心臟切片中不可逆轉細胞損傷的早期檢測：Gb3 包涵體形成前的觀察

Chung-Lin Lee, Dau-Ming Niu

李忠霖 牛道明

Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Department of Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan, ROC

Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

國立陽明交通大學 臨床醫學研究所

臺北馬偕紀念醫院 小兒科部

臺北榮民總醫院 兒童醫學部

Fabry disease (FD) is a lysosomal storage disorder that affects multiple organs, including the heart. The typical pathological hallmark of FD is the presence of globotriaosylceramide (Gb3) inclusion bodies in affected cells. However, the question remains whether significant cellular stress and irreversible damage occur before the formation of these inclusion bodies.

To address this question, we investigated early-stage Gb3 accumulation in fibroblasts from FD patients and myocardial biopsies from G3Stg/GLAko mice and FD patients. Importantly, all biopsies showed detectable Gb3 accumulation under immunofluorescent (IF) staining but lacked the typical FD pathology of Gb3 inclusion bodies. We used IF staining and Western blotting to assess markers of inflammatory and oxidative stress, including interleukin-18 (IL-18), p42/44 mitogen-activated protein kinase (MAPK), and inducible nitric oxide synthase (iNOS). Additionally, we performed IF staining for alpha-smooth muscle actin (α-SMA) to detect the presence of myofibroblasts, which are indicative of fibrosis.

Our results showed that fibroblasts from FD patients, as well as cardiomyocytes from both G3Stg/GLAko mice and FD patients, exhibited significant accumulation of inflammatory markers such as IL-18 and p42/44 MAPK, and the oxidative stress marker iNOS. Furthermore, despite the absence of typical FD pathology, we confirmed the presence of fibrosis in myocardial biopsies from these patients through strong positive staining of α-SMA.

These findings suggest that significant cellular stress and even irreversible damage may occur in the cardiomyocytes of FD patients before the onset of typical pathological changes. This highlights the importance of early intervention in FD patients to prevent irreversible damage and improve their prognosis. Based on our results, we propose that treatment should be initiated much earlier than currently recommended to optimize patient outcomes.

In conclusion, our study provides new insights into the early pathogenesis of FD in the heart and underscores the need for early detection and intervention to prevent irreversible cellular damage. These findings have important implications for the management of FD patients and may guide future research and treatment strategies.

Newborn screening and treatment of lysosomal storage diseases in Japan

日本溶酶體儲積症的新生兒篩檢及治療現況

Kimitoshi Nakamura
中村公俊
Department of Pediatrics, Kumamoto University Graduate School of Medical Sciences, Japan
日本熊本大學 醫學院 小兒科

Management of inborn errors of metabolism is changing from diet therapy and supportive therapy to enzymes and coenzymes replacement, removal of harmful substances, cell and organ transplantation, and gene therapy. In order to effectively perform these treatments, it is important to diagnose inborn errors of metabolism, which is a rare disease, at an early stage. Also, it is necessary to predict severity and prognosis to optimize the treatment. Neonatal screening is effective for the early diagnosis of inborn errors of metabolism. In recent years, the diseases to be found from the neonatal screen have expanded due to an increase in treatable diseases. Tandem mass screening and screening for lysosome disease are good examples. Genetic analysis is indispensable for these definitive diagnoses. As a result of genetic analysis, it is possible to predict the onset time and complications, and begin the necessary treatment at the optimal period. However, confirmed diagnosis by genetic analysis has restrictions in terms of cost, time, and efficiency, and ethical consideration is also required. It is important to carry out genetic analysis while conducting genetic counseling as necessary. Also, in treatment, transplantation therapy and gene therapy become possible, and the importance of genetic knowledge is even higher. I will introduce new diagnosis and treatment of inborn errors of metabolism available in Japan and importance of understanding of genetic background.

Update on diagnosis, enzyme replacement therapy for Pompe disease and gene replacement therapy for spinal muscular atrophy in Vietnamese patients

越南龐貝氏症診斷、酵素替代療法以及脊髓肌肉萎縮症的基因替代療法的最新進展

Vu Chi-Dung

Vietnam National Children's Hospital, Vietnam

Center for Medical Genetics/Genomics, Metabolism, Endocrinology and Molecular Therapy

Department of Clinical Genetics/Genomics and Molecular Therapy

越南國立兒童醫院

醫學遺傳 / 基因組學、代謝、內分泌和分子治療中心

臨床遺傳 / 基因組學和分子治療科

The population in Vietnam was reported 100.3 million inhabitants and number of births was about 1.042 million as of 2023. The rare disease service was set up at the Northern referral center of Pediatrics – Vietnam National Children's Hospital (NCH), Hanoi officially. The NCH in Ha Noi provides services to the population of north Vietnam (~30 million people) for common conditions in children and for rare genetic diseases in whole country. The diagnostic, referral and management workflow for children with neuromuscular disorders including Pompe disease (PD) and spinal muscular atrophy (SMA) is evolving, particularly as newborn screening programs are expanding in tandem with novel therapeutic developments such as enzyme replacement therapy (ERT) and gene therapy.

PD is a rare genetic disorder with an autosomal recessive inheritance pattern and a metabolic consequence. PD birth prevalence is 1:18,711 births (5.3 per 100,000 births) in the dataset of over 11.6M newborns screened for Pompe across 22 states and 8 countries on 4 continents between 2010 and 2022. SMA is caused by a loss or mutation in the survival motor neuron 1 gene (SMN1) on chromosome 5q13, which leads to reduced SMN protein levels and a selective dysfunction of motor neurons. SMA is an autosomal recessive, early childhood disease with an incidence of approximately 1:10,000 live births and carriers is 1:50 in the population. The first children with SMA and PD were confirmed in Vietnam in 2002 and 2015, respectively. The accumulated number of children with PD was 130 cases from 2015 to 2023 at the NCH and six other general/children's hospitals of the country. The number of children with SMA is 791 cases from 2002 to 2022 at NCH. Newborn screening for 6 lysosomal storage diseases including PD was started at NCH in 2021.

The aim of this report is to highlight the database of PD in Vietnam including distribution of subtypes, phenotype, genotype characteristics, mobility, mortality and outcome of ERT. We also mention on database of SMA including distribution of subtypes, mobility, mortality, natural history, complications, efficacy and safety of intravenous infusion of gene replacement therapy, follow up for 32 cases who are less than 2 years of age) as well as clinical trial of intrathecal gene replacement therapy for SMA cases who are ≥ 2 to < 18 years of age.

Global advancements in newborn genomic screening

新生兒基因組篩檢的全球進展

Nicolas Encina

International Consortium on Newborn Sequencing (ICoNS)

新生兒基因定序國際聯盟

Newborn sequencing (NBSeq) has the potential to offer a lifetime of personalized health care and disease prevention that is specific to each individual genome. When fully realized, NBSeq will mark a disruptive transition into personalized medicine and public health. We established the International Consortium on Newborn Sequencing (ICoNS) in 2022 as the first organization specifically dedicated to communicating and sharing progress and best practices in the implementation of NBSeq. Since its inception with principal investigators from 8 separate groups, ICoNS has grown to hundreds of NBSeq specialists, dozens of global projects and is represented by membership from over 40 countries.

The ICoNS mission is to inform the clinical and public health research and implementation of genomic screening in newborns through the harmonization and aggregation of scientific evidence and resources. In that pursuit, ICoNS has commissioned member-run subcommittees that seek to advance the field in precompetitive areas that benefit the community. A few noteworthy subcommittees are: (1) Gene List Subcommittee (2) Data Sharing Subcommittee, and (3) Policy Subcommittee, with others under review.

ICoNS presents an opportunity to gather multi-disciplinary governmental, academic and industry stakeholders and experts from around the world in order to accelerate and harmonize research progress and real-world implementation in NBSeq. The consortium holds an annual conference in October, with the 2024 event scheduled for October 9-10 in New York City, USA. For more information, go to www.iconseq.org.

Applications of a rapid real time analysis system for whole genome / exome sequencing to clinicians

全基因體 / 全外顯子定序即時分析系統在臨床上的應用

Dau-Ming Niu

牛道明

Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 兒童醫學部 及 國立陽明交通大學 臨床醫學研究所

Precision medicine employs genetic testing to accurately predict, prevent, diagnose, and treat diseases. Genetic testing enhances the precision of medication therapies and identifies individuals at higher risk of cancer, even in the absence of symptoms. The decoding of the human genome and advancements in next-generation sequencing technology have made whole genome sequencing (WGS) and whole exome sequencing (WES) more accessible as routine genetic tests in clinical settings.

As we enter the era of preventive medicine, genetic testing provides individuals with a comprehensive understanding of their physiological state, enabling proactive management of health risks based on test results. WGS can identify genetic variations underlying rare and undiagnosed genetic disorders by analyzing the entire genome. Additionally, WGS reveals genetic variations that influence individual responses to medications, allowing personalized drug selection and dosing for optimal therapeutic efficacy and reduced adverse reactions. It can also be used for carrier screening of genetic diseases, informing reproductive planning and aiding in the prevention of transmitting genetic disorders to offspring. However, processing and analyzing the substantial volume of data generated by these tests poses significant challenges. To address this, we collaborated with a bioinformatics service company to develop a "rapid real-time WES/WGS analysis system" that integrates gene analysis technology, cloud computing, big data, and artificial intelligence. This system expedites and ensures accurate diagnoses for patients with genetic diseases, featuring a user-friendly interface and encompassing diverse analyses, including pharmacogenomics, constitutional analysis, proactive analysis, and HLA typing analysis, among others. Furthermore, the system incorporates a genomic AI analysis system (Strata Finder) for assessing the risk of complex diseases, accurately predicting conditions like asthma, acute myocardial infarction (AMI), and stroke with a 99% or higher accuracy rate.

By promoting precision medicine in Taiwan, the system aims to actualize the principle of "prevention is better than treatment" in public healthcare. As technology continues to advance and costs decrease, the clinical applications of WGS are expected to expand further in the future.

Comprehensive analysis of whole cancer genome

癌症基因體的全面分析

Jan-Gowth Chang

張建國

Office of superintendent, Hualien Tzu Chi Hospital, Hualien, Taiwan, ROC

花蓮慈濟醫院 顧問

Cancer is a complex and heterogeneous disease, which affects nearly all organ systems in human body. Both genetic and non-genetic factors contribute to cancer initiation and progression. The pathophysiology of cancer has made huge progress in recent years due to analyze the results of cancer genomes from many large scale sequencing projects, especially the projects of The Cancer Genome Atlas (TCGA) and the ICGC/TCGA Pan-Cancer Analysis of Whole Genomes (PCAWG). These progresses have a marked impact on the cancer drug development and therapeutic approaches for cancer patients, and they are the key of precision oncology. Now, we treat the cancer patients according to the alterations of their cancer genomes, and the core of drug development is to target these alterations. Recently, Taiwan's government also put more efforts for the clinical use of these fields, and will give an imbursement for cancer genome tests in addition to targeted therapy.

Cancer is difficult to cure for the patient with metastatic disease. Many strategies have been used to treat these patients, and the results are always disappointing, and it is an unmet need for cancer patients. Traditional Chinese Medicine (TCM) has been used for the treatment of many types of diseases including cancer, and many evidences have shown to be a new approach for the cancer therapy. In this talk, I will provide a new proposal of cancer treatment based on the integration of TCM and Western Medicine after comprehensive analysis of cancer genome, and databases from TCGA and TCM.

Pompe disease : Now and future

龐貝氏症的現在與未來

Chia-Feng Yang
楊佳鳳
Pediatric Genetic and Endocrinology Division, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 兒童醫學部 遺傳內分泌科

Starting enzyme replacement therapy (ERT) before severe irreversible muscular damage occurs is important in infantile-onset Pompe disease (IOPD). This long-term follow-up study demonstrates our diagnostic and treatment strategies for IOPD and compares our clinical outcomes with those of other medical centers. Out of 1,228,539 infants screened between 1 January 2010 and 28 February 2021, 33 newborns were diagnosed with IOPD in Taipei Veterans General Hospital. Twenty-six patients received regular treatment and monitoring at Taipei Veterans General Hospital.

Echocardiographic parameters, biomarkers, IgG antibodies against alglucosidase alpha, pulmonary function variables, and developmental status were all assessed regularly over an average follow-up duration of 6.18±3.14 years. We compared the long-term treatment outcomes of our patients with those of other research groups. The average age at initiation of ERT in patients with classic IOPD was 9.75±3.17 days. The average of the latest antialglucosidase alpha IgG titre was 669.23±1159.23. All enrolled patients had normal heart sizes, motor milestones, cognitive function and pulmonary function that were near-normal to normal. Compared with patients in other studies, our patients had better outcomes in all aspects. Very early ERT using our rapid diagnosis and treatment strategy allows our IOPD patients to have better outcomes than patients at other medical centers.

Eighteen years later, a new generation of intravenous enzyme replacement therapy (ERT), Nexviazyme, was launched. The efficacy of Nexviazyme in treating Pompe disease was validated in Comet-study involving 100 patients, randomized to receive either Nexviazyme or another FDA-approved enzyme replacement therapy for Pompe disease, Myozyme. On January 21, 2022, the Taiwan Food and Drug Administration added it as an option for Pomope disease, and it will be included in health insurance benefits from April 2023.

All current IOPD and LOPD (late-onset Pompe disease) patients under treatment at our hospital have been successfully switched to Nexviazyme for ERT from Aug 2023. The study aims to analyze patients with Pompe disease treated with this new ERT drug, comparing clinical performance metrics during treatment with Myozyme and after switching to Nexviazyme.

Newborn screening programs for mucopolysaccharidoses Types I, II, IVA, and VI in Taiwan and the application of gene variants

臺灣的黏多醣症第一、二、四A、六型新生兒篩檢計畫與基因變異之應用

Hsiang-Yu Lin, Shuan-Pei Lin

林翔宇 林炫沛

Division of Genetics and Metabolism, Department of Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan, ROC

馬偕紀念醫院 兒童遺傳學科

Background: Mucopolysaccharidoses (MPSs) are lysosomal storage diseases caused by genetic defects that result in deficiency of one specific enzyme activity, consequently impairing the stepwise degradation of glycosaminoglycans (GAGs). Except for MPS II, the other types of MPS have autosomal recessive inheritance in which two copies of an abnormal allele must be present in order for the disease to develop.

Methods: The nationwide newborn screening programs for MPSs were implemented in August 2015, and as of March 2024. 778,341, 667,447, 291,790, and 527,031 newborns have been screened for MPS I, II, IVA, and VI, respectively. A total of 372 suspected infants, including 12 MPS I, 254 MPS II, 106 MPS IVA, and 21 MPS VI, who were referred for MPS confirmation from newborn screening centers in Taiwan, were enrolled. The confirmatory methods used in this study included Sanger sequencing, next-generation sequencing, leukocyte enzyme fluorometric assay, and GAG-derived disaccharides in urine using tandem mass spectrometry assays.

Results: Six, twelve, and 10 infants were diagnosed with MPS I, II, and IVA, respectively. The incidences of MPS I, II and IVA were estimated to be 0.77, 1.80 (3.46 in male), and 3.43/100,000 live births, respectively. Two MPS I, six MPS II, and five MPS IVA had received enzyme replacement therapy, including three MPS II also received hematopoietic stem cell transplantation. We investigated 113 gene variants from infants identified through the newborn screening programs for MPS I, II, IVA, and VI in Taiwan, of which 40 were classified as being pathogenic, 40 as likely pathogenic, 23 as uncertain significance, and 10 as benign, according to the guidelines published by the American College of Medical Genetics and Genomics (ACMG). We also present data including biochemical and molecular DNA analyses, and in vitro gene expression analysis using a COS-7 cell transfection experiment, to define the effect of a variant on the disease itself. The severity of MPS is closely related to variation pattern, i.e., missense, nonsense, small deletion, inversion, splicing, and silent mutations.

Conclusions:A greater understanding of the genotype-phenotype correlations can help predict the severity and prognosis of individual MPS types correctly, and also prompt intensive and long-term follow-up to monitor the health conditions of highly suspected infants.

Spinal muscular atrophy: Now and future

脊髓性肌肉萎縮症的現在與未來

Ting-Rong Hsu
許庭榕
Department of Pediatrics, Taipei Veterans General Hospital, Taipei , Taiwan, ROC
臺北榮民總醫院 兒童醫學部 兒童神經癲癇科

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 the absence of a fully functional motor neurone protein gene that produces the survival motor neurone (SMN) protein. SMN protein encoded by two SMN genes: the SMN1 gene, which is the SMA-determining gene, and the SMN2 gene. Patient with SMA was observed due to the absence of the SMN protein, mostly due to deletion or mutation of SMN1.

Since SMA screening of our hospital started from August 2017 at Taipei Institute of Pathology and Chinese Foundation of Health, several individuals with suspected SMA were found. With newborn screening, we can have the opportunity to get the first symptoms of these patients under the regular and closed monitoring plan. Early treatment could be obtained when the children have symptoms. Spinraza®, the first FDA-approved therapy for SMA, is a treatment that targets the SMN2 gene. Spinraza® is an antisense oligonucleotide approved for all ages and types of SMA. Antisense drugs are small snippets of synthetic genetic material that bind to ribonucleic acid (RNA), so they can be used to fix the splicing of genes like SMN2. A gene therapy called “Zolgensma®” has been approved by the U.S. Food and Drug Administration (FDA) for infants under two years of age with all types of SMA. It is a one-time intravenous (IV) infusion. Evrysdi®, an FDA-approved therapy for the treatment of SMA in all ages and all types, is another treatment that works by correcting the splicing of SMN2. Evrysdi® is a small molecule that is taken daily by mouth or by g-tube.

Several children with SMA have received individual therapy at our hospital. The closed and regular monitoring plan leads to early treatment and excellent outcomes. With the long term prognosis and outcome, the current treatment strategy, multidisciplinary teamwork, and further treatment show important. In this section, we will discuss about the now and the future of patients with spinal muscular atrophy.

Duchenne muscular dystrophy: Now and future

裘馨氏症的現在與未來

Wen-Chin Weng

翁奴謹

Department of Pediatric Neurology, National Taiwan University Children's Hospital, Taipei ,Taiwan, ROC

國立臺灣大學醫學院附設醫院 兒童醫院 兒童神經科

Duchenne muscular dystrophy (DMD) is an X-linked debilitating muscular disorder caused by mutations in the dystrophin gene, resulting in muscle fiber necrosis with progressive replacement by fats and fibrotic tissue. Affected boys may have delayed motor milestones and develop progressive muscle weakness. Currently, there is no curative treatment for DMD and glucocorticoids, primarily prednisolone and deflazacort, are the only medications that are shown to slow the decline in muscle strength and improve function in DMD. When DMD is left untreated, patients with DMD inevitably develop loss of mobility, respiratory and cardiac deterioration in consequence of dystrophic changes of muscle.

In addition to motor and cardiac symptoms, cognitive impairment of varying degree is also common in DMD patients. Considering the multi-organ involvement with variable phenotype, the importance of standardized multidisciplinary care for DMD has been highlighted. Over the years, we have conducted multidisciplinary care for DMD patients to hold back the disease progression, to preventively lessen risk of sequelae, to delay pulmonary and other organ decline, and to improve quality of life of patients.

Although there is no cure other than glucocorticoids that can slow down the deterioration, several potential therapies are under investigation, including exon-skipping strategies, stop codon read-through, gene addition or editing therapy, etc. It is unlikely that any of them when used in isolation will be able to halt or reverse the pathological process of DMD although these therapies are expected to slow disease progression. Effective treatment for DMD is likely to require combinations of therapies that address both the primary defect and its secondary consequences. Although these innovative treatments show potential, the future will likely bring more challenges that will demand more efforts.

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病毒性肝炎、肝癌與門脈高壓：
診斷與治療的永續創新

Viral Hepatitis, Liver Cancer, and Portal Hypertension: Sustainable Innovations in Diagnosis and Treatment

時　間：113年6月22日　08:30-17:25
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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

病毒性肝炎、肝癌與門脈高壓：診斷與治療的永續創新
Viral Hepatitis, Liver Cancer, and Portal Hypertension: Sustainable Innovations in Diagnosis and Treatment

The role of HBV in hepatocarcinogenesis

B 型肝炎在肝癌發生中的角色

Chau-Ting Yeh
葉昭廷
ISCTCR, Chang Gung Memorial Hospital, Taoyuan, Taiwan, ROC
長庚紀念醫院 內科部 胃腸肝膽科

The role of HBV in oncogenesis of liver cancer has long been supported by epidemiological data, including serological evidence and viral load association. Subsequently, it was found that antiviral therapy significantly reduced liver cancer development and neonatal vaccination program significantly reduced liver cancer occurrence in children. Molecular oncogenesis investigation reveals that HBV-hepatocarcinogenesis can be caused by multiple mechanisms: (i) expression of wild type or mutant viral proteins, including X or X truncation proteins, pre-S2 truncation or S truncation proteins, and large (pre-S1) protein; (ii) integration of HBV genomic DNA into critical chromosomal sites; (iii) host genomic mutations caused by hepatocyte proliferation; (iv) microenvironmental changes including inflammatory cells and immune factor changes, epigenetic changes, and others. Recent studies also suggested contribution roles of lncRNA, miRNA, cccDNA, and microbiota in HBV-hepatocarcinogenesis. Most convincing experimental evidence comes from transgenic mice models, although it is unknown how big the gap is between mice and human in terms of hepatocarcinogenesis. Other experimental approaches include survival correlation and tumor growth promoting effects in cell-based and xenograft models. The latter methods can lead to arguments that the proposed mechanisms are in fact cancer growth-maintaining/promoting factors instead of hepatocarcinogenetic factors. Finally, recent studies suggested that prolonged antiviral treatments without complete suppression of HBV might lead to selection of oncogenic HBx mutants. Further investigation is required to confirm/reject the latter argument.

The cons and pros of antiviral therapy for patients in the gray zone

抗病毒藥物對不典型 B 型肝炎患者治療的利弊

Grace Lai-Hung Wong
黃麗虹
The Chinese University of Hong Kong
香港中文大學 內科及藥物治療學系

Chronic hepatitis B virus (HBV) infection is a highly dynamic chronic disease which evolves over decades into different phases, traditionally labelled as immune tolerant phase, immune active phase, and inactive phase. Yet, a significant number of patients with chronic hepatitis B do not align with these well-defined phases, leading to a category known as the gray zone, in which patients do not fulfill the specific criteria for any of the recognised phases. Consequently, under current guidelines, patients in gray zone often do not receive antiviral therapy, presenting unique challenges in their treatment and care. With evolving evidence, key international societies are now in the process of updating their clinical practice guidelines on HBV. The experts around the world are making every effort to improve the management of this complex and dynamic chronic infection which may lead to cirrhosis and its complications, hepatocellular carcinoma (HCC), and hence causing substantial morbidity and mortality. In the last versions of the key international guidelines, treatment indications were defined according to the degrees of viral replication (i.e., serum HBV DNA level) and liver inflammation (i.e., serum alanine aminotransferase [ALT] level). The cutoff value for HBV DNA is often set at 2,000 IU/mL, as patients with such viral load above this cutoff are at increased risk of developing liver cirrhosis and HCC according to the landmark REVEAL study published two decades ago. On the other hand, serum ALT may fluctuate over time and not reflect hepatic necroinflammatory activity reliably, especially in patients with hepatitis B e antigen (HBeAg)-negative CHB, and hence been challenged as a reliable indicator of antiviral therapy. In this lecture, the latest evidence of then natural history and the pros and cons of antiviral therapy on gray zone is discussed.

Finite therapy versus continuous NUCs therapy for patients with chronic hepatitis B

慢性 B 型肝炎抗病毒藥物停藥或長期用藥的利弊

Yao-Chun Hsu

許耀峻

E-Da Hospital, I-Shou University, Kaohsiung, Taiwan, ROC

義大醫院 研究部

義守大學 醫學研究所

Chronic hepatitis B (CHB) remains a major threat to public health around the world, including Taiwan. Nucleos(t)ide analogues (NUCs) have been the mainstay of treatment for CHB, effectively suppressing viral replication and reducing the risk of liver-related complications. However, the optimal duration of NUCs therapy remains a topic of debate. This speech aims to discuss the advantages and disadvantages of finite therapy compared to continuous NUCs therapy in patients with CHB.

Current guidelines recommend indefinite NUCs therapy for most CHB patients, as it has been shown to reduce the risk of hepatocellular carcinoma (HCC) and improve overall survival. Despite the benefits of long-term NUCs therapy, seroclearance of hepatitis B surface antigen (HBsAg) rarely occurs with this approach, raising the concerns of various drawbacks of lifelong treatment. In contrast, finite therapy, which involves discontinuing NUCs after a defined period of viral suppression, has been proposed as an alternative approach to induce HBsAg seroclearance.

This speech will review the current evidence from clinical trials and observational studies to examine the rates of sustained viral response, HBsAg loss, and HBeAg seroconversion, as well as the incidence of virological relapse, biochemical flares, and liver-related complications after NUCs discontinuation. The speech will also cover factors that predict different outcomes following NUCs cessation.

In conclusion, the speaker will provide a comprehensive overview of the current evidence and future perspectives on finite therapy versus continuous NUCs therapy for patients with CHB, with the goal to help optimize treatment strategies and improve clinical outcomes for individual patients.

The risk of HCC after HBsAg seroclearance or HCV clearance after antiviral therapy

B 型肝炎表面抗原廓清或 C 型肝炎治癒對肝癌的影響

Ming-Lung Yu

余明隆

National Sun Yet-sen University, Kaohsiung,Taiwan, ROC

Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung,Taiwan, ROC

國立中山大學

高雄醫學大學附設醫院

Both hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are significant global health threats, contributing to the development of hepatocellular carcinoma (HCC), a prevalent human cancer with high mortality. The progression from chronic viral infection to HCC can span several decades and is affected by various factors such as age at infection, viral genotype, comorbidities, environment and liver fibrosis. While universal HBV vaccination has substantially decreased HBV infection rates and HCC incidence, currently, no vaccine exists for HCV. Hence, effective antiviral therapy plays a pivotal role in HCC prevention, encompassing the treatment of chronic HBV infection and achieving sustained virological response (SVR) in HCV infections.

Eradicating HCV through SVR or sustained suppression of HBV replication has been demonstrated to reduce the incidence of HCC and liver-related mortality. Nevertheless, the risk of HCC remains after viral suppression or even viral eradication. Factors like preexisting liver cirrhosis and age are generalized recognized as contributors to HCC risk among individuals with suppressed HBV or achieved HCV SVR. Epigenetic modifications, including alterations in H3K27ac, have been linked to increased expression of oncogenes and decreased tumor suppression genes, further elevating the risk of liver cancer post-SVR.

Several risk factors associated with post-SVR HCC have been identified, including advanced fibrosis, diabetes, alcohol consumption, higher bilirubin levels, persistent high FIB-4 scores, elevated baseline alpha-fetoprotein (AFP) levels, and specific host genetic variations (MICA, PNPLA3, MBOAT7, TM6SF2, and GCKR). Moreover, metformin and statins have exhibited potential chemopreventive effects against HCC development among HCV-cured or HBV-suppressed patients, as indicated by large-scale cohort studies.

In summary, while significant strides have been made in reducing the burden of HCC through HBV vaccination and effective antiviral therapy, challenges persist in preventing HCC among individuals with viral infections. Unraveling the underlying mechanisms and identifying surrogate biomarkers associated with HCC risk in individuals with viral suppression can inform the development of effective follow-up strategies. Continued research efforts and comprehensive approaches are imperative to further mitigate the burden of HCC among individuals with chronic HBV and HCV infections, including surveillance, risk stratification, and targeted interventions for high-risk populations.

The role of albumin in critically ill cirrhotic patients

白蛋白在病危肝硬化病患的角色

Ming-Hung Tsai

蔡銘鴻

Division of Gastroenterology, Chang Gung Memorial Hospital, Chang Gung University, Taoyuan, Taiwan, ROC

長庚紀念醫院 胃腸肝膽科

Albumin is synthesized by liver and secreted into circulation. Albumin has multiple biological functions. Albumin contributes to 75-80 % of the plasma oncotic pressure because of its molecular mass and negative charge. Because of these oncotic effects, albumin has been used as a volume expander. In fact, albumin infusion is recommended to prevent or treat some complications of decompensated cirrhosis based on its ability to expand plasma volume, including circulatory dysfunction after large-volume paracentesis, and hepatorenal syndrome. In addition to its effects on oncotic pressure, it may serve as a radical scavenger, antioxidant, and immune modulator.

With the progression of liver cirrhosis, albumin decreases in quantity and quality. In patients with acute decompensation and acute on chronic liver failure, toxic oxidized isoforms of albumin increase significantly. Albumin infusion in such subgroups of patients may be beneficial. However, the optimal dosage and frequency of albumin infusion have not yet been defined. Removal of the dysfunctional and toxic isoforms by albumin dialysis may be helpful in some clinical settings. Further investigations are needed. Albumin therapy is not without adverse effects. Pulmonary edema may develop in cirrhotic patients with limited cardiac reserve especially in the setting of acute and short-term treatment for cirrhotic patients with acute decompensation and acute on chronic liver failure.

Precision medicine, multi-omics, and big data in chronic liver diseases

精準醫療、多體學及大數據在慢性肝病的應用

Tung-Hung Su

蘇東弘

Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei,Taiwan,ROC

臺灣大學醫學院附設醫院 內科部 胃腸肝膽科

Liver diseases present a significant global health challenge, necessitating innovative and comprehensive approaches to understanding and managing these conditions effectively. The convergence of cutting-edge technologies drives a paradigm shift in liver disease research and treatment.

Omics refers to high-throughput technologies such as genomics, proteomics, transcriptomics, and metabolomics, enabling researchers to analyze the complete set of molecules within biological samples. These tools offer invaluable insights into the molecular mechanisms underlying liver diseases, identifying disease-specific biomarkers and therapeutic targets, thus facilitating personalized treatment strategies.

With the digitalization of medical records, electronic medical records become a valuable database for big data research. Through reasonable data management and curation, retrospective cohorts are generated to provide real-world evidence to address questions that clinical trials cannot answer. Insights from medical big data also support the design of prospective studies to validate important ideas.

These novel approaches empower researchers and clinicians to unravel the complexities of liver diseases and develop more effective therapeutic interventions.

Abstinence in alcoholic liver disease

酒精性肝病患者的酒癮戒治

Chih-Wen Lin

林志文

Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan, ROC

義大醫院 義守大學 內科部 胃腸肝膽科

Alcoholism remains a major cause of liver disease and is a global health problem worldwide. Alcoholic liver disease (ALD) encompasses a spectrum of injury including steatosis, hepatitis, hepatitis on cirrhosis, and cirrhosis. ALD can lead to fibrosis, cirrhosis, HCC, and mortality. Economic progress has led to an increase of alcohol consumption and changes in drinking behavior, which have resulted in an increased number of cases of ALD in Taiwan. Taiwan has a high prevalence of hepatitis B viral (HBV) infection and hepatocellular carcinoma (HCC) with increasing consumption of alcohol. Our previous study demonstrated that heavy alcohol consumption with ALDH2 polymorphism was associated with increased incidence of HCC and mortality in patients with HBV-related cirrhosis and abstinence from alcohol was associated with reduced risk of HCC and mortality in patients with cirrhosis with HBV infection and alcoholism. Abstinence from alcohol is the cornerstone of treatment and should be recommended to all patients with ALD. Abstinence reduces the risk of HCC, hepatic decompensation and death in cirrhosis patients. Multiple treatment modalities are available, including behavioral therapy, peer-led support programs, and pharmacotherapy. In patients with ALD, the combination of comprehensive medical care and psychosocial interventions are more likely to result in abstinence, and integrated care approaches are associated with better outcomes. Recently, acamprosate, disulfiram and naltrexone are approved by the US FDA and European Medicines Agency for use in alcohol use disorder (AUD). Acamprosate has evidence of efficacy in AUD and is not recommended in Child–Pugh C cirrhosis. Naltrexone is well tolerated in compensated cirrhosis, but dose-dependent hepatotoxicity has been demonstrated in obesity trials and monitoring of liver function tests is recommended. Disulfiram can also lead to hepatotoxicity and is not recommended in advanced liver disease. In summary, abstinence reduces the risk of hepatic decompensation, HCC, and mortality in ALD patients. The combination of comprehensive medical care, pharmacotherapy, and psychosocial interventions are more likely to result in abstinence.

Microbiota in portal hypertension and HCC

腸道微菌叢在門脈高壓及肝癌的角色

Pei-Chang Lee

李沛璋

Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 胃腸肝膽科

Humans harbor nearly 100 trillion gut bacteria that contribute to digestion and intestinal homeostasis. The diverse composition and stable amount of gut microbiome are also essential to keep systemic homeostasis and modulate the innate and adaptive immune systems. Dysbiosis, defined as the imbalance between protective and harmful bacteria both in quality and quantity, and the alteration of intestinal homeostasis will lead to many disorders. Considering 75% of hepatic blood is supplied by the portal vein that not only carries nutrients, but also translocated microbial products and bacteria; gut dysbiosis is considered to participate in the pathogenesis of hepatic steatosis, inflammation and fibrosis via the process of bacterial translocation and multiple interactions with the host's immune system. The alteration of microbial composition and function was also reported to worsen the portal hypertensive complications or even contribute to the hepatic carcinogenesis. Besides, some evidences imply that gut microbiota would have the potential to modulate tumor responses to immunotherapies. In this topic, we will review the microbiota–liver axis and its therapeutic potential in cirrhotic portal hypertension and hepatocellular carcinoma (HCC).

Management of portal hypertension in patients with HCC

肝癌患者門脈高壓之治療

Wen-Chi Chen

陳文誌

Division of Gastroenterology and Hepatology, Department of Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC

高雄榮民總醫院 內科部 胃腸肝膽科

Portal hypertension (PHT) and hepatocellular carcinoma (HCC) are among the major complications of cirrhosis. The prognosis of portal hypertension has improved in these decades. Nevertheless, coexitence of PHT and HCC remains a challenging issue, especially in the era of novel systemic therapies for HCC. In patients with early HCC, PHT ranged from 35% to 52%. In patients with advanced HCC, the prevalence is probably higher than in early HCC. HCC could increase portal pressure through the presence of arteriovenous shunting within the tumor and modifications of liver architecture.

The presence of HCC is associated with a poor prognosis in patients with gastroesophageal varices. Both the risk of bleeding and the rebleeding rates are high in the presence of HCC, especially in the presence of portal vein thrombosis. In the setting of primiary prophylaxis of variceal bleeidng, endoscopic variceal ligation (EVL) is superior to propranolol in patients with HCC. The benefits of EVL on esophageal variceal bleeding and overall survival may be limited to patients with BCLC stage A/B but not to those with BCLC stage C/D. Secondary prophylaxis of acute variceal bleeding was associated with decreased need of transfusion and improved survival, which is more prominent in Child A and B class patients. Transjugular intrahepatic porto-systemic shnunt could be considered when needed in cirrhotic patients with Milan-In HCC to improve survival and as a bridge to liver transplant.

In the HCC patients receiving atezolizumab-bevacizumab treatment, bleeding events were more frequently observed than sorafenib. Banding ligation is indicated in both primary prophylaxis and seconcary propbylaxis of variceal bleeding. A 4-week ligation interval is usually recommended because of the concern of delay post-banding ulcer healing in patients on bevacizumab. Primary prophylaxis should be started before initiation of systemic therapy. In case of portal vein thrombosis, anticoagulant therapy, including new oral direct-oral anticoagulants, are not contraindicated.

Malnutrition, frailty, and sarcopenia in patients with portal hypertension and HCC

營養不良、虛弱及肌少症對門脈高壓及肝癌的影響

Jennifer C. Lai

Department of Hepatology and Liver Transplantation, University of California, San Francisco

加州大學舊金山分校 肝臟及肝移植部

Cirrhosis predisposes patients to malnutrition, frailty, and sarcopenia. While these constructs are interrelated and, in practice, are often recognized simultaneously in a single patient, these constructs have distinct operational definitions: 1. Malnutrition represents the imbalance of nutrients that causes measurable adverse effects on the body and/or outcomes; 2. Frailty is the phenotypic representation of impaired muscle function; 3. Sarcopenia is the phenotypic representation of loss of muscle mass. One can appreciate that malnutrition is a dominant factor that can lead to the clinical phenotypes of frailty and sarcopenia, but there are other many other contributing factors.

Many tools exist to measure frailty and sarcopenia in patients with cirrhosis in clinical practice. The only cirrhosis-specific tool is the Liver Frailty Index, comprised of hand grip strength, chair stands, and balance. Sarcopenia can be assessed using psoas or skeletal muscle index on cross-sectional imaging, although other methods such as bioelectrical impedance analysis (BIA), thigh ultrasound, and dual-energy X-ray absorptiometry (DXA) can be used. Numerous studies have demonstrated strong association of either frailty or sarcopenia with adverse outcomes in patients with cirrhosis, in excess of underlying liver disease severity, portal hypertensive complications, and severity of HCC.

What makes frailty and sarcopenia such a valuable predictor of adverse outcomes is that it is potentially modifiable—and even preventable—with interventions targeted at nutrition and movement. Improving frailty and sarcopenia have been associated with improved outcomes in patients with cirrhosis.

Updates in prediction and management of HCC recurrence after curative treatment

肝癌治癒後再復發的預測及治療

I-Cheng Lee

李懿宸

Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 胃腸肝膽科

The risk of hepatocellular carcinoma (HCC) recurrence remains notably elevated following curative treatment, with rates nearing 60% to 70% at the 5-year mark post-treatment. Identifying patients at high risk of recurrence has emerged as a pivotal concern for guiding adjuvant therapy. HCC recurrence is commonly categorized as either early recurrence (within 2 years post-treatment) or late recurrence (occurring after 2 years). Tumor-related factors such as size, number, microvascular invasion, and AFP levels are established predictors of early recurrence, while host and viral factors like liver fibrosis, inflammation, and viral activity commonly predict late recurrence. Recent advancements have unveiled several novel biomarkers, encompassing both serum biomarkers and molecular signatures, which exhibit correlations with HCC recurrence. Leveraging these predictors, various prognostic models have been introduced to forecast HCC recurrence. The advent of artificial intelligence (AI) and machine learning (ML) technologies has ushered in a new paradigm in HCC diagnosis and management. Recent investigations have underscored the superior predictive efficacy of AI-derived models over conventional clinical models in anticipating HCC recurrence. Encouraging results from the IMbrave050 trial have highlighted the efficacy of adjuvant immunotherapy in high-risk patients post-curative treatment. Concurrently, numerous clinical trials exploring adjuvant and neoadjuvant therapies aimed at mitigating HCC recurrence risk are underway. This lecture aims to provide an updated overview of recent strides in predictive biomarkers, prediction models for HCC recurrence post-curative treatment, and the landscape of adjuvant and neoadjuvant therapies for HCC management.

Refining treatment strategies in intermediate-stage HCC in the era of immunotherapy

免疫治療在中期肝癌的角色

Hideki Iwamoto

Kurume University School of Medicine, Kurume, Japan

久留米大學 內科部 胃腸科

Background

The paradigm shift has happened in the treatment of hepatocellular carcinoma (HCC) due to the development of systemic chemotherapies. As the 1st-line therapy, immune-combination therapy including atezolizumab plus bevacizumab is mainly used. And as the effective anti-angiogenic drug, lenvatinib is also used. A decade ago, the treatment for intermediate HCC is very limited, the only treatment was transcatheter arterial chemoembolization (TACE). However, now we have many therapeutic choices. Therefore, treatments for intermediate HCC are becoming complicated. In the era of chemo-diversity, we need to find the best therapeutic strategy for intermediate HCC.

In the era of chemo-diversity, the main therapeutic strategy is sequential drug therapy. In sequential drug therapy, we need to know how to maximize the effects of each drug and which drugs should be used in sequential drug therapy. In this presentation, I would like to introduce how to maximize the effects of lenvatinib and atezolizumab plus bevacizumab combination therapy and the effects of altering tumor immune microenvironments (TIME) in each systemic drug and locoregional treatments including TACE and HAIC.

Results

＜ Lenvatinib ＞

To maximize the effects of lenvatinib, refinement of the administration schedule is important. Generally, lenvatinib is administered every day without any rest. However, the 5 days-on/2 days-off method, the weekends-off method, is useful for maintaining anti-tumor effects with tolerability. And combination with TACE is also useful to aim for complete response and maintenance of treatment duration of lenvatinib. A combination therapy of lenvatinib and TACE can be used for TACE unsuitable or refractory HCC to aim for a complete response.

＜ Atezolizumab plus Bevacizumab ＞

To maximize the effects of ATZ+BEV, we need to know about the management of adverse events (AEs) in ATZ+BEV. The AEs of special interest in ATZ+BEV are gastrointestinal (GI) bleeding and proteinuria, which are bevacizumab-related AEs. We should have an endoscopy criteria before administration of ATZ+BEV and have to prevent GI bleeding from oesophageal varix. To manage bevacizumab-related AEs, there are two effective methods, BEV-skipping and BEV-dose reduction.

Immune combination therapy is becoming a main actor in the treatment of HCC, and the TIME is attracting attention. Recent studies reveal that tyrosine kinase inhibitors including lenvatinib and

locoregional treatments including TACE and hepatic arterial infusion chemotherapy (HAIC) can alter the TIME from Immune “cold” to “hot”.

Conclusion

In the treatment of intermediate HCC, TACE is still at the center of treatment. However, to maximize the effects of each treatment, we need to understand more about systemic chemotherapies.

Intra-arterial therapy for HCC

肝癌的經動脈給藥治療

Po-chin Liang

梁博欽

Division of Abdomen Radiology, Department of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan, ROC

臺灣大學醫學院附設醫院 醫學影像部

Intra-arterial therapy for HCC, cover wide range from BCLC stage 0~C. TACE is usually indicated for intermediate stage HCC with palliative intent, However, for very early or early HCC, superselective TACE with PV visualization can achieve curative effect, if not suitable for ablation, resection or transplantation. Otherwise, TAE with lipiodol tagging for HCC, followed by ablation is also with curative intent. DEB-TACE is suggested for BCLC B2 substage with bilobar multiple HCCs, or with severe side effect of cTACE. Y90 SIRT(or TARE) can play a role in early HCC with curative intent with radiation segmentectomy, if not suitable for ablation, resection, or transplantation. Y90 SIRT also can be bridging to transplantation to reduce dropout from waiting list, or downstaging to resection or ablation with the added benefit of achieving hypertrophy of the future liver remnant. Y90 SIRT can be salvage after TACE failure for intermediate stage HCC. For BCLC C stage HCCs with branch PV thrombosis, Y90 SIRT can have survival benefit , if refractory to systemic therapy. HAIC with infusion chemotherapy agent into hepatic artery, to increase local treatment effect, and decrease systemic side effect, and because no embolization of hepatic artery, so it is also suitable for HCC with main PV thrombosis. Now Atezo-Bev is 1st line systemic therapy for advanced and certain intermediate stage HCC, according to BCLC stage system 2022, with response rate near 30%. HAIC can be salvage if Atezo-Bev failure, either intermediate or advanced stage HCC. Otherwise, combine HAIC with Atezo-Bev as 1st treatment for advanced or intermediate stage HCC, have promising effect in our limited experience, it need further validation in the future investigation.

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耳鼻喉頭頸部微創手術及器官保留治療的最新進展

Recent Advancements in Minimally Invasive Surgery and Organ Preservation Therapy in ENT and Head & Neck Regions

時 間：113年6月22日 08:35-17:10
Time：June 22, 2024 08:35-17:10

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

耳鼻喉頭頸部微創手術及器官保留治療的最新進展
Recent Advancements in Minimally Invasive Surgery and Organ Preservation Therapy in ENT and Head & Neck Regions

Current updates on office-based procedures in rhinology

鼻科門診手術之最新進展

Li-Ting Hung

洪莉婷

Rhinology Division, Department Otolaryngology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部 鼻頭頸科

With advances in endoscopic instrumentation and technology, recent years have significant expansion in office-based rhinology. The progression of the specialized equipment and novel therapies specifically designed for use in the clinical setting has enabled an increasing number of rhinologic procedures to be effectively performed in the office without the need for general anesthesia. Less-invasive therapeutic options for the management of a broad range of sinonasal pathologies can be performed. Many sinonasal conditions can now be safely and successfully treated in the clinic. Potential advantages in comparison with surgery, such as faster scheduling, shorter procedure duration, quicker patient recovery, and reduced anesthetic morbidity has been noted. These advantages can be related to better satisfaction, less cost, and time saving for both the patient and surgeon. In this review, office-based procedures such as inferior turbinate reduction, balloon-assisted ostium dilation, and cryotherapy would be discussed.

Transnasal approach for orbital / peri-oribtal pathologies

經鼻路徑處理眼及眼周邊病灶

Yu-Wen Huang

黃毓雯

Department of Otolaryngology, Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

The intricate anatomy and close proximity of the nasal and orbital cavities present unique challenges and opportunities for rhinologists in the management of orbital and peri-orbital pathologies. The transnasal approach represents a paradigm shift in the surgical management of orbital and peri-orbital pathologies, offering minimally invasive access to these delicate regions through the natural corridors of the nasal cavity. By harnessing endoscopic techniques and advancements in imaging technology, rhinologists can navigate complex anatomy with precision and achieve optimal outcomes while minimizing morbidity.

Key considerations in the transnasal approach include patient selection, preoperative assessment, and surgical technique. Understanding the nuances of orbital anatomy and pathology is paramount, as it informs decision-making and facilitates tailored surgical interventions. Collaboration with ophthalmologists and neurosurgeons further enhances the multidisciplinary approach to patient care, ensuring comprehensive evaluation and management.

This talk will explore the expanding repertoire of transnasal procedures for a diverse range of orbital and peri-orbital pathologies, including orbital tumors, vascular lesions, and inflammatory conditions. Case illustrations will highlight the efficacy and safety of the transnasal approach in achieving complete resection and optimizing functional and cosmetic outcomes.

In conclusion, the transnasal approach heralds a new era in ophthalmic surgery, empowering rhinologists to address complex orbital and peri-orbital pathologies with greater efficacy and reduced morbidity. Through ongoing innovation and collaboration, we can continue to advance patient care and improve outcomes in this challenging yet rewarding field.

Transnasal approach for sinonasal / skull base malignancies

透過經鼻途徑方式處理鼻腔鼻竇及顱底惡性腫瘤

Chien-Fu Yeh

葉建甫

Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

Sinonasal and skull base malignancies pose a complex and demanding array of tumors with distinctive anatomical considerations and clinical features. Originating from diverse tissues within the sinonasal and skull base regions, such as the nasal cavity, paranasal sinuses, and neighboring structures like the orbit and intracranial compartment, these malignancies present unique challenges. Treatment typically involves a multidisciplinary approach integrating surgery, radiation therapy, and chemotherapy, tailored to the specific tumor type, location, and disease extent. Recent advancements in surgical methods, and supplementary therapies have contributed to enhanced outcomes in patients with these malignancies. Nonetheless, achieving optimal results hinges on precise diagnosis, thorough surgical planning, and comprehensive postoperative management.

The transnasal approach has emerged as a valuable method for treating sinonasal and skull base malignancies. This technique presents various benefits, such as providing direct access to tumors situated in intricate anatomical areas while reducing damage to nearby tissues. This section explores the fundamental principles, surgical methods, and results linked with employing the transnasal approach to manage these malignancies. Moreover, it underscores the significance of interdisciplinary cooperation in enhancing patient outcomes and reducing postoperative complications. In summary, the transnasal approach shows promise as a comprehensive treatment strategy for sinonasal and skull base malignancies, offering enhanced surgical accessibility and potentially improved patient results.

Challenges and strategies in managing Eustachian tube dysfunction

耳咽管功能障礙的挑戰與應對策略

Chien-Yu Hsueh

薛健佑

Department of Otorhinolaryngology, Head & Neck, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

The Eustachian tube serves as a conduit between the middle ear and nasal cavity, approximately 3 to 4 centimeters long, composed of bone, cartilage, and soft tissues. Its primary functions include regulating middle ear pressure, clearing secretions, preventing bacterial migration, and shielding the inner ear from noise. Dysfunction can lead to symptoms like ear fullness, pain, tinnitus, and echoing voices. Types of dysfunction include obstructive, baro-challenge-induced dysfunction, and patulous. Diagnosis involves medical history, endoscopy, and hearing tests. Treatments vary by cause. For obstructive dysfunction, medication or balloon eustachian tuboplasty may be effective. Patulous dysfunction, less responsive to medication, might require middle ear ventilation tube placement or surgical valve implantation to promote closure. Accurate diagnosis is crucial for effective treatment.

Advancements in minimally invasive middle ear surgery: My personal experience

發展中耳微創手術的個人經驗

Tzong-Yang Tu
杜宗陽
Department of Otorhinolaryngology, Head & Neck, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 耳鼻喉頭頸醫學部

In the late 1990s, I initiated my personal transcanal tympanoplasty technique that involved direct access through the drum perforation under a microscope. This technique reached maturation in the mid-2000s and was subsequently introduced to the otologic community and the public. Surgical results are shown to illustrate the efficacy of this method in treating lesions efficiently while preserving normal tissue structure and function.

Endoscopic middle ear surgery gained prominence worldwide in the early 2010s, with several renowned otologists advocating its adoption. The author incorporates endoscopic components not only in otitis media but also in cholesteatoma and otosclerosis operations. A comprehensive approach, utilizing both endoscope and microscope, is emphasized for its versatility and potential advantages.

I introduced a novel approach by combining the endoscope and microscope in middle ear surgery. While acknowledging the prevalent use of endoscopes at 0, 30, and 45-degree angles, the author prefers a more versatile utilization. This approach has proven beneficial, particularly in advanced ear surgery such as successful repair of skull base defects with cartilage and reducing complication and recurrence rates.

The combination of endoscope and microscope, termed bi-scopic surgery, has become the author's routine practice, even in challenging cases such as cholesteatoma with skull base invasion, congenital cholesteatoma, and otosclerosis operations. The report emphasizes the efficiency of this approach, resulting in shorter operation times, improved hearing outcomes, and lower recurrence rates.

The author recommends the use of a 70-degree endoscope, rarely mentioned by other otologists. The large angle of this endoscope facilitates clear identification and removal of cholesteatoma matrix, especially in advanced cases, further contributing to the success of the surgical intervention.

The integration of transcanal tympanoplasty and endoscopic components in middle ear surgery represents a significant advancement in otologic practice. The author's versatile approach, combining both endoscope and microscope, offers a comprehensive solution with potential benefits in various otologic procedures. This report encourages further exploration and adoption of these techniques within the otologic community.

Office-based laryngeal surgery

門診喉部手術

Yen-Bin Hsu

許彥彬

Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部 喉頭頸科

Benign laryngeal lesions are common in laryngology clinic. Traditionally, many of these lesions are treated surgically, mainly in the operating room under general anesthesia. However, this procedure requires complex instruments and carries the risk and costs associated with general anesthesia. Additionally, patients with C-spine disease and trismus are not ideal candidates for this surgical procedure.

With the advancement of endoscopes in ENT field, laryngologists can obtain a better view of the vocal folds. Office-based laryngeal surgery has become increasingly popular over the past two decades. In our hospital, transoral laryngeal surgery under flexible laryngoscopic guidance has been carried out since 1993. Initially, we conducted transoral injection laryngoplasty for patients with unilateral vocal fold paralysis. With increasing experience, we expanded our procedures to include biopsies of laryngeal or pharyngeal lesions, removal of foreign bodies, and phonosurgery for vocal fold polyps, all performed transorally. Since 2007, we have also been performing corticosteroid injections for the treatment of benign laryngeal lesions, such as vocal fold polyps, nodules, cysts, and vocal process granulomas, using a percutaneous approach via the cricothyroid or thyrohyoid membranes.

Currently, office-based laryngeal surgery has become an important treatment modality in the field laryngology. It has spared many traditional surgeries, allowing patients to save valuable time and expenses associated with hospital admission and general anesthesia. In this section, we will share our experiences in performing office-based laryngeal surgery, including patient outcomes, and discuss its benefits and limitations.

Interventional sialendoscopy for patients with radioiodine induced sialadenitis: Experience at Taipei Veterans General Hospital

以唾液腺內視鏡手術治療放射性碘引發之慢性唾液腺炎：臺北榮總治療經驗

Chia-Fan Chang

張嘉帆

Department of Otorhinolaryngology, Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

國立陽明交通大學 醫學院 醫學系

臺北榮民總醫院 耳鼻喉頭頸醫學部

Background: Radioiodine therapy has been proven to be an effective treatment for patients with differentiated thyroid cancers following total thyroidectomy. However, a known consequence of this therapy is radioiodine-induced sialadenitis (RAIS), which significantly distresses patients. Interventional sialendoscopy, a minimally invasive surgical procedure, has been introduced for the management of RAIS. The aim of this study is to analyze the treatment result at our hospital and compare them with previous literature reports.

Methods: Patients with RAIS who underwent interventional sialendoscopy between January 2014 and January 2022 at Taipei Veterans General Hospital were recruited. Demographic and clinical data were collected, including age, gender, symptoms, dosage of radioiodine therapy, gland involvement, surgical indications, intraoperative findings, procedures, complications, and patient satisfaction.

Results: Thirteen patients with RAIS were analyzed. Ten patients were female, and three were male. The mean age was 49.16 years (range, 37.95-77.79 years). Six patients underwent more than one surgical procedure. Symptoms were more commonly related to the parotid gland (92.31%) than the submandibular gland (7.69%). Both sides of the glands were affected in six patients (46.15%). Stenosis was the most common intraoperative finding. At the last postoperative follow-up, nine patients (69.23%) still experienced varying degrees of salivary gland symptoms, but reported feeling better than before surgery.

Conclusion: Interventional sialendoscopy could serve as an effective tool for managing patients with RAIS who do not respond to conservative treatment.

Clinical applications of minimally invasive techniques in the management of thyroid nodules: Emphasizing radiofrequency ablation and ethanol injection

甲狀腺結節低侵入性治療的臨床應用：專注於射頻消融和乙醇注射術

Tsung-Lun Lee

李宗倫

Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

Thyroid nodules are a common clinical finding, with an estimated prevalence of 50% in the general population. While the majority of thyroid nodules are benign and asymptomatic, a subset may require intervention due to symptoms or suspicion of malignancy. Conservative management of thyroid nodules has gained significant attention in recent years, reflecting a shift towards non-invasive interventions to address the common clinical entity. This approach is particularly valuable in cases where surgical intervention may pose a higher risk to the patient or when individuals prefer non-surgical treatments due to various reasons such as cosmetic concerns or underlying health conditions that make surgery less favorable. Two prominent modalities within non-invasive treatment are radiofrequency ablation (RFA) and ethanol injection (EI), both offering minimally invasive options with promising outcomes.

RFA has garnered interest for its efficacy in reducing the size of thyroid nodules and alleviating associated symptoms. The use of thermal energy to target and shrink nodules has not only shown promising outcomes in clinical studies but has also provided a minimally invasive option for patients who may not be suitable candidates for surgery. Moreover, the ability of RFA to improve patient-reported outcomes adds to its appeal as a valuable tool in the management of symptomatic thyroid nodules.

Similarly, EI has emerged as a viable approach, particularly for thyroid nodules with cystic components. By inducing necrosis and subsequent volume reduction through direct injection of ethanol, this technique offers a safe and effective alternative to surgery. The ability of EI to not only reduce nodule size but also alleviate symptoms and improve cosmetic outcomes further enhances its significance in the conservative treatment of thyroid nodules.

As research continues to validate the efficacy and safety of these non-surgical interventions, it is evident that RFA and EI are likely to play an increasingly vital role in comprehensive patient care. The ability to tailor treatment options according to individual patient needs and preferences while ensuring effective management of thyroid nodules underscores the importance of these minimally invasive techniques in the modern healthcare landscape.

Tongue conservation treatment by neoadjuvant chemotherapy followed by surgery and risk-adapted adjuvant therapy for oral tongue squamous cell carcinoma: A phase II clinical trial

以前置式輔助性化學治療、手術及風險適應輔助治療進行舌癌的舌保留治療：第二期臨床試驗

Shyh-Kuan Tai

戴世光

Department of Otolaryngology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

國立陽明交通大學 耳鼻喉科

Background: To assess the feasibility of tongue conservation treatment with induction chemotherapy (ICT), tongue conservation surgery, and risk-adapted postoperative adjuvant therapy in oral tongue squamous cell carcinoma (OTSCC).

Methods: Patients with newly diagnosed OTSCC cT2-4 N0-2 M0 were recruited. The ICT with a regimen of docetaxel, cisplatin, and oral tegafur/uracil (DCU) was administrated every 21 days. After the first cycle of ICT (DCU1), patients with a more than 30% decrease in the longest diameter of primary tumor underwent a second cycle of ICT (DCU2). Tongue conservation surgery was performed after ICT, and risk-adapted adjuvant therapy was organized based on pathological features.

Results: From July 2011 to December 2015, a total of 23 patients were enrolled, 87% of whom were classified as stage III–IV. Clinical responders to DCU1 and DCU2 were determined in 90.5% (19/21) and 88.2% (15/17) of patients. Tongue conservation surgery was performed in 16 responders to ICT. Only one patient had a positive margin (6.3%), and a complete pathologic response was achieved in eight patients (50%). Only one patient developed local recurrence after a median follow-up of 58.6 months (range, 7.9–105.2). The 5-year overall survival (0% vs. 87.5%, $p = 0.001$) and disease-specific survival (0% vs. 93.3%, $p = 0.000$) were significantly different between the DCU1 non-responders and responders.

Conclusion: Tongue conservation treatment with ICT, followed by conservation surgery and risk-adapted adjuvant therapy, is feasible for patients with OTSCC who are good responders to ICT. However, the outcomes of non-responders are dismal. Further study in a larger patient population is warranted.

Customizing an irradiation-free therapy for squamous cell carcinoma of oropharynx: Feasibility or fiction

口咽部鱗狀上皮癌無放射線的個人化治療：現實或想像？

Yaoh-Shiang Lin

林曜祥

Department of Otorhinolaryngology-Head and Neck Surgery, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC

高雄榮民總醫院 耳鼻喉頭頸醫學部

In recent years, the incidence of oropharyngeal cancer caused by human papillomavirus (HPV) infection has risen sharply in European and American countries. These account for about 70% of the annual oropharyngeal cancer cases. Taiwan has also witnessed a gradual increase of HPV-related oropharyngeal cancer incidence, but these account for only about one-quarter of the annual oropharyngeal cancer cases. The remaining three-quarters of cases were still attributed to smoking, alcohol, and betel nut use.

Traditionally, the majority of oropharyngeal cancer patients received concurrent radiotherapy and chemotherapy. This achieved relatively good treatment outcomes, but lead to considerable long-term sequelae in the survivors' lives. HPV-related oropharyngeal cancer tends to respond better to radiotherapy and chemotherapy. Therefore, various de-escalation therapies were explored worldwide to reduce treatment sequelae and improve the quality of life of these patients.

However, the majority of oropharyngeal cancer cases in Taiwan are caused by smoking, alcohol, and betel nut use. This report will share the experience of our hospital in recent years in implementing de-escalation therapy for oropharyngeal cancer cases (mainly tonsillar cancer and base of tongue cancer).

Neoadjuvant chemotherapy followed by transoral laser microsurgery for laryngopharyngeal cancers: Changing NACT regimen from TPF to DCU

前導式化療後施行經口雷射顯微手術應用於咽喉癌之治療：從 TPF 到 DCU 處方

Pen-Yuan Chu

朱本元

Department of Otolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 耳鼻喉頭頸醫學部

國立陽明交通大學 耳鼻喉科

Traditionally, total laryngectomy has been the standard treatment approach for advanced laryngeal and hypopharyngeal cancers. However, this method results in the loss of the larynx, leading to a deterioration in the quality of life for patients. Over the past two decades, a combination of chemotherapy and radiotherapy (CRT) has become more popular, but high severe late toxicities have been reported, including laryngeal and pharyngeal dysfunction.

Transoral laser microsurgery (TLM) has emerged as an alternative organ-preserving treatment method for several decades. Initially applied primarily to early-stage cancers, with the introduction of the concept of neoadjuvant chemotherapy (NACT), TLM is now being utilized for advanced-stage laryngeal and hypopharyngeal cancers. The main purpose of using NACT is to induce tumor shrinkage, followed by TLM to excise the tumor with margins adjusted according to the extent of the shrunken tumor. This approach may reduce the need for postoperative radiotherapy (RT) or decrease the RT dosage if necessary, potentially enhancing the quality of life after treatment.

Since 2016, two cycles of NACT with the docetaxel, cisplatin, and 5-fluorouracil (TPF) regimen or cisplatin and 5-fluorouracil (PF) regimen have been administered for bulky laryngeal and pharyngeal tumors. The clinical response rate of primary tumors can achieve up to 89% (16/18), including a 33% complete response and a 56% partial response rate. However, patients receiving NACT with TPF or PF regimens require hospitalization for at least 5 days. Furthermore, 66% of the patients experienced severe neutropenia (grade 3 and 4).

In recent years, the NACT regimen has shifted from the TPF regimen to the DCU regimen (docetaxel, cisplatin, and Ufur) for two cycles. The advantages of the DCU regimen include outpatient department (OPD) treatment, no need for port-A insertion, comparable tumor response (95%), and a lower rate of severe neutropenia (18%). Most of the tumors can be excised with en bloc resection under TLM after NACT.

This presentation will share our experiences with NACT followed by TLM for laryngeal and pharyngeal cancers.

Transoral robotic surgery for laryngeal and hypopharyngeal cancer

經口機器人手術應用於喉癌及下咽癌

Chen-Chi Wang

王仲祺

Department of Otolaryngology Head &Neck Surgery, Taichung Veterans General Hospital, Taichung , Taiwan, ROC
School of Medicine, National Yang Ming Chiao Tung University, Taipei , Taiwan, ROC
臺中榮民總醫院 耳鼻喉頭頸醫學部
國立陽明交通大學 醫學院

After the da Vinci robotic surgical system gained widespread adoption among cardiothoracic and urologic surgeons for assisting in endoscopic procedures, its application has expanded to include the treatment of head and neck diseases. This robotic-assisted technique offers several distinctive features, such as a 3-D high-magnification endoscope and endo-wristed instruments equipped with motion scaling and tremor reduction functions. These advancements enable surgeons to execute endoscopic surgeries with enhanced precision, dexterity, and control.

In the ENT field, one of the rapidly emerging robotic surgical procedures is transoral robotic surgery (TORS), particularly for treating upper airway diseases such as early-stage pharyngeal and laryngeal cancers. Common surgical indications include oropharyngeal tumors affecting the palatine tonsil, tongue base, and supraglottis. However, we have expanded the application of TORS to include the management of hypopharyngeal cancer, glottic carcinoma with anterior commissure involvement, and even total laryngectomy.

Based on our published papers and prospective studies, TORS has demonstrated the potential to provide patients with favorable survival rates, local control rates, and organ preservation rates, along with satisfactory outcomes in swallowing and phonation. Moreover, TORS has shown promise in reducing surgical morbidities, allowing a significant portion of our patients to either avoid radiation therapy altogether or receive reduced dosages. In this presentation, I will share my experiences with TORS by presenting relevant data. I will discuss the advantages of TORS and delve into its implications. However, the da Vinci robot comes with a high price tag, and consequently, the cost of TORS remains high in Taiwan, with the procedure not covered by the National Health Insurance system. To further advance head and neck robotic surgery, ongoing collaboration, and communication among experts from around the globe are essential.

The role of immunotherapy in non-metastatic head and neck cancer

免疫治療在非轉移頭頸癌的角色

Muh-Hwa Yang
楊慕華
Division of Medical Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 腫瘤醫學部

Immune checkpoint inhibitors (ICI) have brought about a paradigm shift in the treatment landscape of recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). ICI monotherapy or in combination with chemotherapy is now considered the standard of care for first-line treatment of R/M HNSCC, while ICI monotherapy has also gained approval as the standard treatment for platinum-refractory R/M HNSCC. However, the role of ICI in locally advanced HNSCC has been explored to a limited extent. Pivotal clinical trials have failed to demonstrate the efficacy of ICI in combination with definitive concurrent chemoradiotherapy (CCRT), with potential explanations including the lymphatic system damage caused by definitive CCRT, which may dampen the antitumor immune response. In addition to chemo-immuno-radiotherapy, extensive clinical trials are underway to investigate the role of ICI as neoadjuvant treatment before definitive therapy. Additionally, there is accumulating evidence from studies examining the role of ICI as adjuvant therapy following post-operative CCRT. In summary, ICI has heralded a paradigm shift in the treatment of HNSCC, with its role in R/M HNSCC now well established. Further translational studies are needed to elucidate the underlying mechanisms responsible for the ineffectiveness of the ICI-CCRT combination, as well as clinical trials aimed at elucidating the role of ICI in earlier stages of HNSCC, such as neoadjuvant or adjuvant treatment.

Carbon ion radiotherapy for head and neck cancer: Initial experience of Taipei Veterans General Hospital

碳離子放療應用於頭頸癌：臺北榮總初步經驗

Ling-Wei Wang, Yu Mei Kang, Yu Wen Hu

王令瑋 康鈺玫 胡育文

Institute of Heavy Ion and Radiation Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 粒子及放射腫瘤部

Surgery and radiotherapy (RT) are both important modalities for head and neck squamous cell carcinoma (HNSCC). Intensity modulation radiotherapy with photon is the standard of care for HNSCC. However, for pathology other than SCC in the head and neck region, the results of photon RT are often unsatisfactory. Particle therapy, esp. carbon ion radiotherapy (CIRT), may be one of the choices for uncommon pathology in the H & N region. We started a clinical trial with CIRT at Taipei Veterans General Hospital since 2022 and started regular treatment since May 2023.

From our CIRT databank, we found 6 salivary gland tumors (2 major and 4 minor), one ameloblastoma and one SCC of maxillary sinus. Among them 4 were males. Acute toxicities were all mild (grade 1-2). Most tumors had response (including 4 CR) to CIRT with our limited follow-up time. For late toxicity, one patient had carotid blowout syndrome. One patient had soft tissue necrosis. The case with maxillary sinus cancer had recurrence 5 months after CIRT. All patients survived up to this presentation.

Our initial experience demonstrates that CIRT is an effective modality of Rx for head and neck cancer other than HNSCC with mild acute toxicities. However, few patients still had grade 3 late toxicity. Enrollment of more patients and longer follow up are needed

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榮總三總中研院合作研究計畫成果發表會

Result Presentations of the Cooperative Research Project of Taipei Veterans General Hospital, Tri-Service General Hospital, and Academia Sinica

合辦單位：臺北榮民總醫院
協辦單位：臺中榮民總醫院、高雄榮民總醫院、三軍總醫院、
中研院

時　間：113年6月22日　08:30-12:00
Time：June 22, 2024　08:30-12:00

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

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先進數據技術於顱顏面手術之發展

Advanced Image Technology in Craniomaxillofacial Surgery

時 間：113年6月22日 09:00-12:00

Time：June 22, 2024 09:00-12:00

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

先進數據技術於顱顏面手術之發展

Advanced Image Technology in Craniomaxillofacial Surgery

Innovations in craniofacial reconstruction: Leading the future through image-guided surgical simulation, customized implants, 3D printing, intraoperative imaging, and navigation systems

顱顏重建的創新：透過影像引導手術模擬、客製化植入物、3D 列印和手術中成像及導航系統引領未來

Han-Tsung Liao

廖漢聰

Department of plastic surgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan,ROC

林口長庚紀念醫院 整形外科

The field of craniofacial reconstruction has witnessed remarkable advancements with the integration of intraoperative imaging and navigation technologies. This talk explores the transformative impact of intraoperative 3D C-arm CT imaging and navigation systems in conjunction with other cutting-edge methodologies, including surgical simulation, customized implants, and 3D printing guidance, in the context of craniofacial reconstruction procedures.

Intraoperative 3D C-arm CT imaging offers surgeons real-time, high-resolution visualization of the surgical field, providing invaluable insights into anatomical structures and surgical progress. When combined with surgical simulation software, this imaging modality facilitates seamless integration of preoperative plans with intraoperative reality, enabling surgeons to execute complex procedures with enhanced precision and efficiency.

Intraoperative navigation systems complement the capabilities of 3D C-arm CT imaging by providing surgeons with real-time guidance and feedback during surgical procedures. By overlaying preoperative plans onto intraoperative images, navigation systems enable surgeons to navigate complex craniofacial anatomy with unparalleled accuracy, facilitating precise implant placement, bone reshaping, and soft tissue manipulation.

A pivotal component of modern craniofacial reconstruction is the utilization of customized implants. Traditional off-the-shelf implants often fail to adequately address the unique anatomical variations present in craniofacial defects, leading to suboptimal outcomes and increased risk of complications. However, with recent advancements in additive manufacturing technologies, such as 3D printing, surgeons can now fabricate patient-specific implants that precisely conform to the individual patient's anatomy. These customized implants offer superior fit, biomechanical stability, and aesthetic outcomes compared to their generic counterparts, thereby enhancing the overall success of craniofacial reconstruction procedures.

The integration of 3D printing technology into craniofacial reconstruction workflows has been transformative, offering unparalleled levels of customization and versatility. By leveraging patient-specific anatomical data, surgeons can design and fabricate intricate surgical guides and models that facilitate precise intraoperative navigation and streamline complex surgical procedures. Furthermore, the ability to rapidly iterate and customize implant designs based on patient feedback allows for iterative refinement

and optimization of surgical outcomes, ensuring the highest levels of patient satisfaction and functional restoration.

In summary, the integration of intraoperative imaging and navigation technologies with surgical simulation, customized implants, and 3D printing guidance represents a paradigm shift in craniofacial reconstruction. These synergistic approaches empower surgeons with enhanced visualization, precision, and control, leading to improved patient outcomes and satisfaction. As we continue to push the boundaries of technological innovation, the future of craniofacial reconstruction holds promise for even greater levels of surgical success and patient care.

Computer - assisted craniofacial surgery

電腦輔助顱顏手術

Thomas Mon-Hsian Hsieh

謝孟祥

Center for Craniofacial Medicine & Morphological Sciences, National Taiwan University Hospital , Taipei, Taiwan, ROC

Division of Plastic surgery, National Taiwan University Children's Hospital, Taipei, Taiwan, ROC

臺灣大學醫學院附設醫院 顱顏醫療暨形態科學發展中心

臺灣大學醫學院附設兒童醫院 重建整形外科

Surgeries over the craniofacial region are challenging, as they pose the characters of small and well-hidden incisions - therefore limited operation field, and the exist of nearby vital structures like vessel, nerve, eyeballs and brain. Even more difficult on the occasion of congenital anomalies treatment. With the advance of the computer technology, now we can use modern medical imaging techniques to assist these challenging procedures. They include: Surgical Navigation System and CAD/CAM technology. We can use them on pre-op design and simulation, intra-op guides and assisted in implant and cutting guide fabrication. With the help of these techniques, we can perform the craniofacial procedure more precisely, efficient and safe, and the results could be more predictable and satisfactory.

The use of augmented reality for flap perforator identification

擴增實境於皮瓣穿通枝辨識的應用

Yu-Chung Shih[a,c]、Wun-Chan Yu[b]、Tien-Hsiang Wang[a,c]

石育仲[a,c] 俞文展[b] 王天祥[a,c]

[a] *Division of Plastic & Reconstructive Surgery, Department of Surgery, Taipei Veteran General Hospital, Taipei, Taiwan, ROC*

[b] *3D Printing Technology and Resource Integration Center, Department of Medical Engineering, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

[c] *School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC*

[a] *臺北榮民總醫院 外科部 重建整形外科*

[b] *臺北榮民總醫院 醫學工程部 3D 列印技術發展暨資源整合中心*

[c] *國立陽明交通大學 醫學院 醫學系*

The identification of flap perforators is important for flap design and harvest. Using medical imaging to assist in precise intraoperative localization of these perforators can reduce surgical time and complications. Though computed tomography angiography (CTA) can provide perforator images and even reconstruct three-dimensional (3D) virtual models of bones and perforating vascular anatomy. However, these images are still confined to screens and cannot be directly displayed in the surgical field, relying solely on the surgeon's mental alignment. Augmented reality (AR) technology, employing computer vision alignment to overlay virtual images onto the surgical field, aids surgeons in a more intuitive interpretation of medical images.

3D virtual anatomical images are reconstructed with 3D Slicer, and the relative position between targeting and virtual images is established by Vuforia. Intraoperative flap perforators identification is done through auto-registration either by image target or model target. The flap perforators are then confirmed during flap dissection. With the reconstructed 3D virtual perforator images, augmented reality is able to locate the flap perforators on the body surface intraoperatively.

Drawing a body blueprint: Experience in virtual surgical planning

描繪人體藍圖：擬真手術計畫的經驗

Tien-Hsiang Wang

王天祥

Division of Plastic & Reconstructive Surgery, Department of Surgery,Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 重建整形外科

With the advancement of 3D printing and virtual surgical planning, including computer-aided design and manufacturing, plastic surgeons now have access to highly precise methods for performing surgeries. Here, we share our experiences with utilizing this technology in nasal augmentation rhinoplasty, genioplasty, and the resection of bony tumors in the zygoma. This approach provides surgeons with well-planned, customized surgical guides tailored to the specific needs and conditions of each patient. These surgical guides are highly reliable, resulting in consistently successful outcomes and reproducible procedures.

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乳癌精準治療：從臨床試驗到真實世界數據

Tailored Treatment of Breast Cancer from Trial-Based and RWD Perspective

時　間：113年6月22日　08:30-12:10
Time：June 22, 2024　08:30-12:10

地　點：臺北榮民總醫院 致德樓第六、七會議室
Place：The Conference Room 6&7, Chih-Teh Building
Taipei Veterans General Hospital

乳癌精準治療：從臨床試驗到真實世界數據
Tailored Treatment of Breast Cancer from Trial-Based and RWD Perspective

Revisiting the landscape of HER2 biology in breast cancer: Insights and perspectives

回顧 HER2 生物學在乳腺癌中的全貌：新見解與觀點

Chun-Yu Liu
劉峻宇
Division of Medical Oncology, Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 腫瘤醫學部

In this topic, we will provide a comprehensive overview of the current understanding and recent advancements in HER2 biology within the context of breast cancer. HER2, a pivotal biomarker and therapeutic target in breast cancer management, has undergone significant scrutiny and exploration over the years. This review revisits the intricate landscape of HER2 biology, shedding light on its role in breast cancer development, progression, and therapeutic resistance. We highlight recent insights into HER2 signaling pathways, molecular mechanisms driving HER2-driven tumorigenesis, and emerging treatment strategies. Furthermore, we discuss the evolving perspectives on HER2-targeted therapies, including novel therapeutic modalities and combination approaches aimed at overcoming resistance and improving patient outcomes. Through a synthesis of current research findings and clinical implications, this review offers valuable insights and perspectives for further exploration and advancement in the field of HER2-targeted breast cancer therapy.

The real-world data of HER2-directed therapy in early breast cancer

早期乳癌使用標靶治療的實境數據回顧分析

Yi-Fang Tsai

蔡宜芳

Comprehensive Breast Health Center & Division of Breast Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 乳房醫學中心 外科部乳房外科

Early-stage HER2-positive breast cancers are largely treated with chemotherapy combined with anti-HER2 therapy. Adjuvant trastuzumab, as the standard treatment since 2006, had markedly reduce recurrence and subsequent mortality in HER2-positve breast cancer. Following the invention of pertuzumab, double blockade of target therapy creates significant progress first in trials of neoadjuvant setting, then in adjuvant setting for node-positive disease. As the raising populations who received neoadjuvant systemic therapy (NST), trastuzumab emtansine demonstrated its efficacy in reducing recurrence for those with residual tumors after NST. The strategy of treatment in HER2-positive early breast cancer is drafted based on mounting evidence from clinical trials and now well accepted by experts. However, regimens of first choice may not be applied to every single patient due to limitation from policy of insurance or individual finance. The side effects of HER2-directed therapy are another concern after the epochal drug had been introduced to clinical practice for nearly two decades. Here we will review the real-world data of anti-HER2 therapy in early breast cancer.

Health-related quality of life in HER2-positive early breast cancer woman using HER2 target therapy

HER2 陽性早期乳癌女性使用 HER2 標靶藥物治療之健康相關生活品質探討

Guo-Shiou Liao

廖國秀

Department of General Surgery Tri-Service General Hospital, Taipei, Taiwan, ROC

三軍總醫院 一般外科

Breast cancer remains one of the most common malignancies affecting women worldwide, with a subset characterized by overexpression of the human epidermal growth factor receptor 2 (HER2). HER2-positive breast cancers are known for their aggressive nature but have seen significant improvements in prognosis and survival outcomes with the advent of HER2-targeted therapies. While the efficacy of these treatments in prolonging life is well-documented, understanding their impact on patients' health-related quality of life (HRQoL) is crucial for holistic patient care.

Explore the HRQoL outcomes associated with various HER2-targeted therapies in women with HER2-positive early breast cancer, specifically comparing Trastuzumab&Pertuzumab (PH) vs. Trastuzumab (H); Trastuzumab emtansine (T-DM1) vs. Trastuzumab deruxtecan (T-DXd), and subcutaneous (SC) vs. intravenous (IV) administration routes.

As the treatment landscape for HER2-positive early breast cancer evolves, so too does our understanding of how these therapies impact patients' lives beyond survival. The current data and research contributes to a growing body of evidence that supports a holistic view of cancer care, where HRQoL is a pivotal consideration in treatment planning. Future research should continue to explore these dimensions, ensuring that advances in cancer therapy translate into meaningful improvements in patients' lives.

Early HER2-positive breast cancer: Who may benefit from neoadjuvant therapy?

術前輔助治療對早期 HER2 陽性乳癌的臨床運用與效益

Chi-Cheng Huang

黃其晟

Breast Health Center & Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 乳房醫學中心

Neoadjuvant therapy has emerged as a crucial approach in managing early HER2-positive breast cancer, aiming to optimize outcomes by downsizing tumors and increasing breast-conserving rates. This therapeutic strategy typically involves a combination of sequential chemotherapy and HER2-targeted therapy, such as trastuzumab. The benefits of neoadjuvant breast cancer treatment, including chemotherapy, endocrine therapy, and targeted therapy, are well-established, contributing to disease downstaging and improved treatment efficacy.

Identification of candidates who may particularly benefit from neoadjuvant therapy in early HER2-positive breast cancer is pivotal. This tailored approach is especially pertinent for cases where downsizing the tumor is crucial for optimal surgical outcomes or breast conservation.

In summary, neoadjuvant therapy plays a vital role in the management of early HER2-positive breast cancer, offering benefits in tumor downsizing and increasing breast-conserving rates. Tailoring this approach to specific patient subgroups, including those with hormone receptor-positive, HER2-negative tumors, enhances its effectiveness in achieving optimal outcome

Striving for significant survival benefit for the broadest set of patients in HR+HER2- mBC with CDK4/6i

臨床積極運用 CDK4/6 抑制劑為 HR+HER2- 轉移乳癌患者群體帶來顯著的生存效益

Jiun-I Lai

賴峻毅

Department Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 腫瘤醫學部

Randomized phase III trials have consistently demonstrated therapeutic benefits with ribociclib to endocrine therapy in HR+ HER2- advanced breast cancer. Across studies in pre- and postmenopausal populations, the ribociclib-endocrine combination improved progression-free survival (PFS) and overall survival (OS) versus endocrine monotherapy, without compromising quality of life (QoL).

Notably, in the RIGHT Choice study of premenopausal patients with aggressive disease features like high visceral burden or rapid progression - typically requiring chemotherapy - the ribociclib regimen with ovarian suppression and an aromatase inhibitor achieved comparable objective response rates and superior PFS compared to standard chemotherapy combinations. These data signal a potential paradigm shift in managing advanced HR+/HER2- disease. While cytotoxic chemotherapy has historically been standard for high tumor burden or visceral crisis, integrating targeted CDK4/6 inhibition into endocrine-based therapy may offer an equally efficacious but better-tolerated strategy, circumventing chemotherapy's deleterious effects on QoL.

As clinical utility of CDK4/6 inhibitors is further elucidated, these agents hold considerable promise in extending survival while preserving QoL, particularly for patients with aggressive, life-threatening manifestations.

Optimizing treatment in patients with HER2-positive early breast cancer by extended adjuvant treatment

用強化輔助治療最佳化 HER2 陽性乳癌患者的治療

Yen-Jen Chen

陳彥蓁

Breast Cancer Center, Taipei Veteran General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 乳房醫學中心

Breast cancer is by far the most frequent disease among women in Taiwan, and the diagnosis and treatment have also been improved a lot these years. HER2, the abbreviation of human epidermal growth factor receptor 2, could be one of the key biological factors in breast cancer category. The overexpression or amplification of HER2 gene could lead to cell abnormal progression, and it accounted for around 20% of breast cancer.

The application of trastuzumab significantly improved the clinical outcome of early stage HER2-positive breast cancer, nevertheless, nearly 30% of patients who had trastuzumab still faced recurrence risk within 10 years. Moreover, there are some other factors, such as nodal status, hormone receptor status, and achieving pCR or not, may influence the risk of recurrence.

Neratinib, an irreversible tyrosine kinase inhibitor, showed its efficacy with a different mechanism from mono-clonal antibodies, making it an option to extend patients' adjuvant treatment with a better outcome, especially for those who had a higher risk of recurrence than others. ExteNET trial demonstrated neratinib lowered 27% of recurrence risk in a 5-year follow-up period. The study also showed that the benefit of extended adjuvant therapy is higher in subgroups with a higher risk, such as non-pCR population.

This benefit has also been recognized by international guidelines, including NCCN, ESMO, and ASCO, suggests that 1-year extended adjuvant treatment should be considered for patients who have a higher risk.

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快速檢測於急診醫療的應用

Application of Rapid Testing in Emergency Medical Care

時　間：113年6月22日　08:30-12:00

Time：June 22, 2024　08:30-12:00

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

快速檢測於急診醫療的應用

Application of Rapid Testing in Emergency Medical Care

Advancing emergency diagnostics: The impact of lateral flow assays

急診診斷進展：側流式檢測

Cheng-Han Chen

陳正翰

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Department of Emergency Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

國立陽明交通大學 醫學院

臺北榮民總醫院 急診部

In the realm of contemporary medical diagnostics, point-of-care testing (POCT) signifies a seminal shift from centralized laboratory paradigms to bedside analyses, catalyzing real-time clinical judgments. This essay will scrutinize the ascendancy and implications of such innovations, particularly through the prism of lateral flow assays (LFAs). LFAs have catapulted to prominence amidst the COVID-19 pandemic, emblematic of rapid, simplistic, and cost-effective diagnostic methodologies. Their pivotal role in expedient disease detection, especially tailored for mass screening and resource-constrained environments, epitomizes the advent of accessible healthcare technology.

The proliferation of COVID-19 antigen LFAs underscores their utility in navigating public health crises. The facility of these assays, necessitating merely a nasal swab and minutes to yield results, has fomented decentralized testing. Consequently, this has expedited case identification, and subsequent isolation and treatment – a linchpin in curtailing the spread of contagion. During the zenith of the pandemic, emergency departments globally were inundated with cases, yet LFAs provided a respite by diminishing wait times and stratifying confirmed cases, alleviating medical infrastructural strains. Reports from Taipei Veterans General Hospital's emergency department corroborate this, aligning with international literature on LFAs' efficacy.

Furthermore, the confluence of portable spectrophotometric technologies with LFAs harbors the potential for enhanced quantitative analysis. In emergency medicine, LFAs are being refined to discern an array of biomarkers – such as interleukin-6 or procalcitonin – pertinent to the severity and monitoring of diseases. The design of LFAs facilitates continual monitoring, bestowing upon healthcare professionals' timely data to inform patient care. This rapid diagnostic capacity is indispensable in acute medical scenarios where temporal economy is paramount, potentially preserving life and ameliorating prognoses.

To encapsulate, the infusion of POCT and LFAs into medical praxis has been transformative, and their prospective evolution promises to amplify their utility. Advancements in sensitivity, specificity, and digital integration anticipate a future where enhanced patient care and outcomes are not aspirational but assured, especially within the exigent confines of emergency departments.

Development of rapid diagnostic tools

新式快速檢測工具開發

Chao-Min Cheng

鄭兆珉

Institute of Biomedical Engineering, National Tsing Hua University, Hsinchu, Taiwan ,ROC

國立清華大學 生物醫學工程研究所

Following the outbreak of COVID-19, a myriad of rapid diagnostic tools emerged and quickly received broad public endorsement. COVID-19 pandemic catalysed a transformative period in the biomedical engineering field, with collaboration between academic researches and medical units accelerating the development of innovative rapid diagnostic tools from academic investigations into how the fundamental principles of infectious diseases, immunology, and bioengineering can be amalgamated to create robust rapid diagnostic tools. The swift development of rapid diagnostic tools post-COVID-19 represents a watershed moment in medical science, where the collaborative efforts of academic researches and practical applications have yielded a suite of tools that are reshaping the landscape of disease diagnosis and treatment monitoring.

I will talk about what we have done in terms of the development of new diagnostic tools for last few years such as COVID-19-relevant diagnostic tools, biofilm diagnostic tool, IL-6 diagnostic tool for disease severity monitoring, but not limited to. I would look forward to exchanging the ideas with audience as well during the lecture.

A paper-based analytical device for analysis of paraquat in urine and its validation with optical-based approaches

尿液巴拉刈紙質檢測裝置與光學法驗證

Tse-Yao Wang

王則堯

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Department of Emergency Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

國立陽明交通大學 醫學院

臺北榮民總醫院 急診部

Background: Paraquat is a highly toxic herbicide, posing a significant public health threat due to its potential for fatal poisoning. The rapid identification and timely treatment initiation based on the accurate analysis of paraquat concentration in urine or serum is crucial for enhancing patient prognosis. However, the conventional methods for measuring paraquat concentration are hampered by their time-consuming nature and the requirement for expensive, bulky equipment.

Methods: In response to these challenges, this study introduces a paper-based analytical device as an innovative diagnostic tool aimed at facilitating point-of-care testing. The device utilizes colorimetric methods for the quantification of paraquat concentration in urine, offering a practical solution to the limitations associated with traditional analytical techniques.

Results: The evaluation of the paper-based analytical device revealed an R^2 value of 0.9989 for the paraquat standard curve, spanning a dynamic range of 0-100 ppm, with a detection limit of 3.01 ppm. Comparative analysis with two other optical-based approaches, Spectrochip and NanoDrop, indicated that the paper-based device's performance is on par with these methods, as supported by Bland-Altman analysis. Clinical validation was conducted using urine samples from six patients with paraquat poisoning, further affirming the device's accuracy and practical utility.

Conclusion: The findings from this study confirm the efficacy of the developed paper-based analytical device in accurately detecting urine paraquat concentration. Its ease of use, efficiency, and comparable performance to other colorimetric methods make it a valuable tool for improving the clinical management of paraquat poisoning. By enabling quicker decision-making in treatment initiation, this device represents a significant advancement in the field of point-of-care diagnostics, potentially leading to better patient outcomes in cases of paraquat poisoning.

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生醫永續：北科生醫健康論壇
2024產學交流平台

Shaping the Future of Sustainable Biomedicine: Intelligent Medicine Conference of Beitou Shilin Biotechnology Park

時　間：113年6月22日　08:30-17:00
Time：June 22, 2024　08:30-17:00

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

生醫永續：北科生醫健康論壇2024產學交流平台

Shaping the Future of Sustainable Biomedicine: Intelligent Medicine Conference of Beitou Shilin Biotechnology Park

Healthcare 4.0: The way towards future care and hospital sustainability

Healthcare 4.0：建構未來智慧與永續醫療的數位基石

Jonney Shih
施崇棠
Chairman, ASUSTek Computer Inc., Taipei, Taiwan, ROC
華碩電腦股份有限公司

The COVID-19 pandemic has significantly impacted the healthcare system, leading to the need for reform and the adoption of new technologies. The future of healthcare will be shaped by three key trends: Precision Health, Virtual Care, and Hospital Resilience. Precision Health is a personalized approach to healthcare that takes into account an individual's unique genetic makeup, lifestyle, and environmental factors. Virtual Care, also known as telehealth, allows patients to receive medical care remotely, using technology such as video conferencing, mobile apps, and wearable devices. Hospital Resilience refers to a hospital's ability to withstand and recover from disruptive events, such as natural disasters, pandemics, and cyber attacks. Hospitals also face severe challenges, including staff shortages exacerbated by the COVID-19 pandemic and highlighted in the 2024 WEF report, concerns about patient privacy amid digitalization, and struggles in economically disadvantaged countries. Additionally, the industry's substantial carbon footprint and other ESG issues pose formidable challenges.

These trends are being empowered by digital technologies, such as Artificial Intelligence (AI), Internet of Things (IoT), and Real-time technologies, which are driving the development of a Healthcare Cyber-Physical System (CPS). The Healthcare CPS is a network of interconnected devices, sensors, and systems that work together to deliver smart, personalized healthcare. The Healthcare CPS is composed of three layers: smart infrastructure, smart platforms, and smart applications. Smart infrastructure is equipped with advanced technologies such as AI, IoT, and real-time monitoring to enable real-time data collection and analysis. Smart platforms refer to the software platforms that enable the integration and analysis of data from multiple sources. Smart platforms use AI and machine learning algorithms to identify patterns and trends in data, enabling healthcare providers to make informed decisions about patient care. Smart applications refer to the software applications that enable healthcare providers to deliver personalized care to patients.

ASUS has been at the forefront of this transformation, providing innovative solutions such as wearables, portable ultrasound devices, xHIS platforms, and AI supercomputers to help hospitals and bio-research institutions navigate these challenges. Moreover, ASUS prioritizes a sustainable strategy, viewing it as essential to core operations. For over two decades, ASUS has transitioned from passive compliance to integrating sustainability into its operations by emphasizing data-driven, scientifically managed sustainability efforts as well as focusing on climate action, circular economy, responsible manufacturing, and value creation.

From enterprise to healthcare: A paradigm shift in sustainability

從企業到醫院的永續典範轉移

Eugene Chien
簡又新
Taiwan Institute for Sustainable Energy, Taipei, Taiwan, ROC
臺灣永續能源研究基金會

Under the global trend of sustainable development and ESG, hospitals and the healthcare industry are gradually shifting towards more responsible business models. Although the healthcare sector started later compared to the corporate world, it has shown significant progress. On the path to net zero in the healthcare industry, the UNFCCC held the first Health Day at the COP28 conference, acknowledging and highlighting the interconnection between climate and healthcare impacts. The carbon footprint of healthcare accounts for 4.6% of Taiwan's carbon emissions and as much as 7.6% in the United States. Many hospitals in the UK and the US have begun implementing green reduction measures to minimize environmental impact, achieving notable results on the path to net zero.

In this era of great transformation, the healthcare system needs to understand and embrace the opportunities brought by the transition to net zero. Since new knowledge and concepts drive industry changes, reforms in on-the-job training, internal training for employees, and lifelong learning initiatives are essential to foster new thinking patterns. Through continuous innovation and improvement, hospitals can not only stand out in the competition but also bring long-term positive impacts to society as a whole. These comprehensive changes provide new directions for the healthcare industry, aiming to play a significant role in the wave of sustainable development.

Promotion and prospects of net-zero policy in health systems

醫療機構推動淨零排放政策與展望

Yue-Ping Liu
劉越萍
Ministry of Health and Welfare, Department of Medical Affairs, Taiwan, ROC
衛生福利部 醫事司

In 2021, during the United Nations Climate Change Conference (COP26), 50 member states signed the "Country commitments to build climate resilient and sustainable health systems" with the aim of achieving net-zero goal for the global health systems by 2050. These commitments entail establishing climate resilient health systems and sustainable low carbon health systems. Notably, there are 16 ambitious member states set specific target years to achieve net-zero, highlighting that the international communities attach great importance to sustainable health systems. Taking the United Kingdom as an example, the National Health Service (NHS) amended the Health and Care Act in 2022 and incorporated response to climate change as a key mission.

In Taiwan, the National Development Council proposed the "Taiwan's Pathway to Net-Zero Emissions in 2050 " in 2022, and the "Climate Change Response Act" was passed on January 10th 2023, stipulating that Taiwan aims to achieve greenhouse net-zero emissions by 2050. This signifies the imperative for all sectors to push for net-zero emissions and places a significant responsibility on the health systems, which serves the dual purposes of promoting high-quality health and care and responding to climate change. The presentation today will begin by sharing insights on international trends in terms of promoting sustainability in health systems, which can serve as a reference for health systems in Taiwan while also providing directions and considerations for future domestic policies.

Share with you : Kaohsiung Veterans General Hospital Experience regarding ESG investment

高雄榮總實踐 ESG 醫院治理之經驗分享

Jin-Shuen Chen

陳金順

Administration Department, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC

高雄榮民總醫院 院本部

Kaohsiung Veterans General Hospital (KSVGH) is the only public medical center in the Kaohsiung-Pingtung District. Under the supervision of the government and the Veterans Affairs Council, KSVGH assumes the three major roles of public hospital, veterans' hospital and medical center in the Kaohsiung-Pingtung District, and continues to fulfill its social responsibilities.

In Taiwan, the operation of the veterans' hospital system is a self-funded operation and is self-sufficient. Its governance principles also need to be similar to corporate governance systems, and be responsible to legal, financial, professional, and policy considerations, and to the public. However, the difference is that hospital governance is a public welfare institution and non-profit organization that serves the general public. In 2020, Taiwan released "Corporate Governance 3.0-Sustainable Development Blueprint", which proposed its core vision as "implementing corporate governance and enhancing the sustainable development of enterprises" and "creating a sound ESG ecosystem and strengthening the international competitiveness of the capital market." In line with national policies, hospital management also needs to keep pace with the times, so that hospitals can develop sustainably.

The main content of this lecture is to briefly describe the similarities and differences between corporate governance and hospital governance, and to review the literature on hospital governance. Next, we will share the process of our hospital following the TW-SDGs goals, our hospital strategies, and our receipt of the 2023 National Sustainability Award. We will conclude by sharing our vision for future development.

Reimagining ESG: Emphasizing demand over cost

重新想像 ESG：不在成本、而在需求

Kuo-Hua Yu
于國華
Research & Development, Taipei National University of the Arts, Taipei, Taiwan, ROC
國立臺北藝術大學

The United Nations has successively proposed CSR, ESG, and SDGs to guide the world towards sustainable development. Among these, both businesses and organizations are increasingly prioritizing ESG.

ESG aims to regulate the deviation in corporate operations that excessively prioritize profit figures. Under the goal of sustainable development, businesses cannot disregard moral and ethical obligations. Corporate operations must incorporate the costs of social responsibility, environmental protection, and ethical corporate governance into their cost plans to demonstrate the true performance of the enterprise.

In fact, apart from the calculation deviation in business operating costs, a more significant reason for the current global ecological and social crises lies in the excessive demand from advanced societies. Unmet demands lead to overconsumption, resulting in societal inequality and an unsustainable burden on the Earth.

Indigenous peoples or many traditional societies possess traditional knowledge. They respect natural ecosystems and pursue reasonable needs, enabling them to maintain ecological and social balance and harmony. The current global emphasis on collective action regarding ESG helps alleviate the pressure and pace of ecological and social destruction. More importantly, it is about how humans can redefine their understanding of needs and control desires, allowing excessive and extremely unfair consumption to return to levels acceptable to both the ecology and society.

ESG serves as an indicator of the civilization level of corporate operations. Another indicator of modern societal civilization is how we learn from traditional societies' ecological ethos and implement sustainable development in our lives.

Health care industry's ESG : An introduction of SASB

醫療機構行業 ESG：簡介 SASB 的規範

Cheng-Ying Shiau

蕭正英

Occupational Safety and Heath Office, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 職業安全衛生室

Corporate Social Responsibility (***CSR***), first coined in the 1950s, is an internal organizational policy or a corporate ethic strategy aiming to make a business accountable. It is a strategic initiative that contributes to a brand's reputation. It became more codified into a set of business practices such as sustainability initiatives in 1990s. ***ESG*** is a set of aspects, including environmental issues, social issues and corporate governance that can be considered in responsible investing / impact investing. ***ESG criteria make business' CSR efforts measurable***. The term ESG first came to prominence in a 2004 report titled "Who Cares Wins", which was a joint initiative of financial institutions at the invitation of the United Nations (UN). Since 2020, there have been accelerating incentives from the United Nations to overlay ESG data with the Sustainable Development Goals (***SDGs***).

Through Corporate Sustainability Report, corporates and organizations communicate and demonstrate accountability for their impacts on the environment, economy and people. Global Report Initiative (***GRI***) provides the world's most widely used sustainability reporting standards. The GRI standards have 3 major parts: universal standards, sector standards and topic standards. GRI sector standards currently support only 4 business sectors, namely "Oil and gas", "Coal", "Agriculture Aquaculture and Fishing", and "Mining".

The Sustainability Accounting Standards Board (SASB) is a non-profit organization, founded in 2011 by Jean Rogers to develop sustainability accounting standards. As would be expected, sustainability issues manifest differently from one industry to another due to differences in business models, resource dependencies, and other factors. SASB's Sustainable Industry Classification System® (SICS®) organizes industries using a combination of traditional classification factors and sustainability risks and opportunities. SASB has developed industry-specific standards for 77 industries across 11 sectors.

Hospital or heath care institutes is one of the 6 businesses in the health care sector, as defined by the SICS of SASB. The industry is characterized by high fixed labor and facilities costs, and an increased regulatory focus on reduced costs of care and improved outcomes. In this talk, the 11 SASB topics for Health Care Delivery will be concisely presented to the audience.

Reimagining healthcare with generative AI: A vision for the future

以生成式人工智慧重塑醫療健康之未來新願景

Ted Chang
張嘉淵
CTO of Quanta Computer Inc.
廣達電腦股份有限公司

The field of artificial intelligence, particularly generative AI, is rapidly evolving and poised to reshape various industries, including healthcare. This keynote speech envisions how generative AI models could serve as a transformative force in reimagining healthcare delivery, accelerating medical research, and enhancing patient outcomes.

Recent advancements in large language models, diffusion models, and other generative techniques have unlocked unprecedented capabilities in creating new data, such as text, images, and audio, based on training datasets. These models possess the potential to revolutionize drug discovery processes, generate personalized educational materials, augment medical imaging analysis, and support clinical decision-making.

This presentation explores the current challenges faced by the healthcare industry, including slow drug development pipelines, limited access to personalized care, and inefficiencies in diagnostic imaging. It then delves into how generative AI could address these challenges, democratizing access to healthcare through tailored virtual assistants and educational resources, while accelerating medical breakthroughs and enhancing diagnostic accuracy.

Furthermore, the keynote envisions how generative AI could integrate with emerging technologies like the Internet of Things and robotics to create new healthcare delivery models. It paints a future where personalized, AI-assisted care plans adapt to individual patient needs, and telemedicine is enhanced by generative AI support for remote patient monitoring.

While embracing the transformative potential of generative AI, the speech also addresses the critical need for robust evaluation, mitigation of biases in training data, and adherence to ethical principles surrounding privacy and responsible use of sensitive medical data. It emphasizes the importance of interdisciplinary collaboration between AI researchers, healthcare professionals, policymakers, and ethicists to maximize the benefits while mitigating risks.

Ultimately, this visionary keynote aims to inspire the audience to actively participate in shaping the future of healthcare, fostering innovation while prioritizing ethics and patient well-being. It calls for a generative revolution that augments human capabilities and paves the way for a future where AI plays a pivotal role in providing better healthcare for all.

Acer Medical: From innovation to implementation

宏碁智醫：從創新到落地

Allen Lien

連加恩

Acer Medical Incorporated, New Taipei, Taiwan, ROC

Acer Incorporated, New Taipei City, Taiwan, ROC

National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

宏碁智醫股份有限公司

宏碁股份有限公司

國立陽明交通大學

Acer Medical, a subsidiary of Acer, leverages artificial intelligence, extensive clinical datasets, and software development capabilities in its operations. Acer Medical remains committed to make AI work for the core needs of humanity by applying AI in healthcare, such as precision medicine, preventive medicine and public health. The company has successfully introduced four medical equipment products, with three of them representing AI image interpretation solutions. Achieving regulatory approvals from both Taiwanese and international regulatory authorities, Acer Medical adheres to the ISO 13485 quality system, meeting rigorous global standards.

Acer Medical remains committed to ongoing collaborative research with its partners, dedicated to ensuring that intelligent and human-centric medical care remains accessible on a global scale.

Digital healthcare transformation with Azure OpenAI: Past, now and coming future

透過 Azure OpenAI 加速數位醫療轉型：過去、現在、與即將的未來

Danny Chen
陳守正
GM of Public Sector, Microsoft Taiwan
臺灣微軟 公共業務事業群

The integration of Generative Artificial Intelligence (AI) presents both opportunities and challenges in revolutionizing the operations of government institutions and healthcare facilities. In the current landscape, these entities grapple with the formidable task of digital transformation. Challenges include outdated infrastructure, data security concerns, and resistance to change within bureaucratic systems.

Generative AI holds immense promise in addressing these challenges by enhancing administrative efficiency for government personnel and boosting productivity for healthcare professionals. Through advanced algorithms and automation, Generative AI streamlines administrative tasks, optimizes resource allocation, and facilitates data-driven decision-making in government agencies. In healthcare settings, Generative AI empowers medical personnel by automating routine processes, assisting in diagnostics, and personalizing treatment plans, thereby improving overall patient care and safety.

Furthermore, Generative AI elevates the quality of public services by enhancing the citizen experience. By analyzing vast datasets and predicting citizen needs, government agencies can tailor services, streamline interactions, and improve accessibility. This personalized approach fosters greater trust in government institutions and enhances overall public satisfaction.

In conclusion, while the implementation of Generative AI in government and healthcare poses significant challenges, its transformative potential cannot be overstated. By addressing these challenges and leveraging the opportunities presented, Generative AI stands to revolutionize these sectors, ultimately improving administrative efficiency, healthcare outcomes, and public service delivery.

5G and AIoT empowering smart healthcare: Creating convenient and high-quality medical services

5G 及 AIoT 驅動智慧醫療應用：打造便捷優質的醫療服務

Tian-Tsair Su

蘇添財

Chunghwa Telecom Laboratories., Taoyuan, Taiwan, ROC

中華電信研究院

The concept of health equity has been widely embraced as a universal value. While Taiwan's medical standards are relatively high, there are still challenges to achieving health equity. These challenges include limited access to healthcare in remote and offshore areas, shortages of healthcare professionals, and rising costs.

Chunghwa Telecom, with its extensive ICT expertise in fixed-line and mobile communications, big data, cybersecurity, the Internet of Things (IoT), and artificial intelligence (AI), is poised to revolutionize healthcare accessibility in Taiwan. We have established a high-coverage wireless communication network, developed a telemedicine platform, and integrated mobile medical devices to support remote consultations, video consultations, and counseling services. These efforts are not just about improving medical care accessibility in remote and offshore areas but also about saving patients time and transportation costs and, most importantly, ensuring they receive high-quality medical care. This is a step towards a future where healthcare is accessible to all, regardless of location.

To address the shortage of healthcare professionals and rising costs, we have developed localized (Mandarin/Taiwanese/English/Hakka) speech-to-text (STT) and generative AI technologies. These technologies are used to create medical AI assistants, intelligent customer service agents, and AI voice assistants for healthcare applications. Our goal is to alleviate the shortage of healthcare workers and reduce hospital operating costs, ensuring the financial sustainability of healthcare in Taiwan.

In the future, we will continue to innovate and develop our technologies. we are establishing develop low earth orbit (LEO) satellite communications to further enhance the coverage of our wireless communication network. Our speech recognition technology will be expanded to support Indonesian and Vietnamese languages for hospital customer service, breaking down language barriers for new immigrants seeking medical care. We will also develop large language models for the medical field, assisting hospitals in creating medical generative AI applications. Additionally, we will provide context-aware, human-like virtual services to support hospital Q&A services, reducing the workload of hospital staff. These future developments reflect our commitment to continuously improve and adapt our technologies to meet the evolving needs of the healthcare industry.

A deep learning model (VeriOsteo® OP) for osteoporosis detection using standard chest X-ray: A multicenter study

胸部 X 光以 AI 預測骨質疏鬆

Cheng-Hung Lee

李政鴻

Central office of Administration, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 院本部

An increasing number of studies are dedicated to the development of deep learning models in medical imaging for Osteoporosis prediction. The Chest X-ray (CXR) serves as a standard examination within routine physical examinations, stands as the most frequently utilized image diagnosis modality. It constitutes a valuable subject for osteoporosis research and prevention. Since T12 and L1 vertebrae are commonly associated with osteoporotic fractures based on previous literature, this study collaborates with Acer Medical Inc. to develop a deep learning model, VeriOsteo® OP, for bone mineral density (BMD) prediction and the identification of individual with high risk of osteoporosis using the image of CXR.

We retrospectively reviewed individuals with age above or equal to 50 who underwent both CXR and Dual-energy X-ray Absorptiometry (DXA) examinations with interval within six months. We excluded individuals with absence of T-score value of L1-L2-L3-L4 or the difference of T-score value between adjacent vertebrae greater than 1. The VeriOsteo® OP contains two Artificial Intelligence (AI) image deep learning models. The first model employs image detection techniques to delineate the T12 and L1 regions on CXR and adjusts the image contrast and window level. Then, upload the extracted image to the second model to predict the averaged BMD value of L1 to L4 vertebrae. Finally, convert the predicted BMD into a T-score value and diagnose Osteoporosis (T-score ≤ -2.5) based on the World Health Organization (WHO) announcement.

This study included 440 patients with a mean age of 62.5. Of 304 patients were from the medical center Taichung Veterans General Hospital (VGHTC) and the other 136 patients were from the community physical examination center Joy Clinic. Male and female comprised 20.2% and 79.8% respectively and 253 individuals (57.5%) were diagnosed as osteoporosis. Significantly correlation (R = 0.88) was found between the BMD values of model prediction and gold-standard DXA measurement. The accuracy of osteoporosis diagnosis (T-score ≤ -2.5) was 88.99% with sensitivity 88.71% and specificity 89.36%. The area under curve (AUC) of osteoporosis diagnosis was 94.61%, which indicates the model have well-performing diagnostic capability.

The proposed model VeriOsteo® OP validated by multicenter data represents a promising and reliable auxiliary tool for the osteoporosis diagnosis using the T12 and L1 image region on CXR. The VeriOsteo® OP provides an opportunity for early detection of osteoporosis and further osteoporosis related fracture prevention.

Voice signals for predicting cognitive impairment in older adults

高齡長者命名測試中語音訊號預測認知功能異常

Liang-Kung Chen

陳亮恭

Taipei Municipal Gan-Dau Hospital (Managed by Taipei Veterans General Hospital), Taipei, Taiwan, ROC

臺北市立關渡醫院 委託臺北榮民總醫院經營

Cognitive impairment, such as Alzheimer's disease, is a growing concern among the aging population. Early detection is crucial for timely intervention and management. However, current diagnostic methods can be invasive, costly, and time-consuming. This study explores the use of voice signals from cognitive assessment recordings as a non-invasive and cost-effective tool for predicting cognitive impairment in older adults.

The study employed a novel approach involving automatic speech recognition (ASR) and machine learning techniques. Voice recordings from cognitive assessment tasks, including fruit/animal fluency tests and news recitation, were collected from older adults at Taipei Veterans General Hospital. The recordings were transcribed using ASR models, and semantic features related to fluency and expressiveness, such as word counts, unique word usage, keyword density, and language perplexity scores, were extracted from the transcripts. These features were transformed into intuitive measures like lexical fluency, lexical richness, speech rate, accuracy, and voice fluency. A Logistic Regression model was trained using these transformed features to predict cognitive impairment status, determined by the Montreal Cognitive Assessment (MoCA) score. To ensure robustness, a five-fold cross-validation technique was employed.

Overall, 115 older adults were enrolled (71 of them were cognitively normal by the MoCA results). The study included data from 161 fruit fluency tests, 119 word card tests, and 149 news recitation recordings. The Logistic Regression models achieved promising performance, with accuracy ranging from 74.49% to 80.67% across different cognitive tasks. The results demonstrated the potential of voice signals as a reliable indicator of cognitive impairment.

This research contributes to the understanding of speech recognition technology's capabilities in semantic comprehension and provides an analytical foundation for further studies in related domains. The proposed method shows promise as a non-invasive and cost-effective tool for early detection of cognitive impairment in older adults, potentially enabling timely intervention and management.

Smart healthcare: Artificial intelligence and big data

智慧醫療：人工智慧與健康大數據

Chien-Yeh Hsu

徐建業

Department of Information Management, National Taipei University of Nursing and Health Sciences, Taipei , Taiwan, ROC

臺北護理健康大學 資訊管理系

Medical information has received much attention in recent years, and its applications have developed very rapidly. The development process of smart medical care is all centered on data. The current trend of medical and health big data is quite consistent with the health cloud promoted by the Ministry of Health and Welfare. The future trend of medical information is based on cloud personal health care. Among them, integrated information communication construction, personal medical health data acquisition, storage, utilization, sharing, protection, and cloud health care services are the main topics of discussion. How to use individual and group health data analysis to promote smart health care is a very important key approach. Topics to be discussed today include: individualized smart and precision medicine and healthcare, analysis and application of huge amounts of medical and health data, international standards for medical information such as HL7 FHIR and its development, infrastructure for health and medical information and the development of electronic medical records, health data processing and value-added application, data governance and personal data protection. It is expected that a complete medical and health care information architecture will be established in the future, using digital technology, data analysis and artificial intelligence to establish prediction models and conduct timely and efficient detection and intervention to achieve personalized precision health care.

Smart hospital development blueprint for Taipei Veterans General Hospital

臺北榮總智慧醫療發展藍圖

Wui-Chiang Lee

李偉強

Deputy Superintendent, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 院本部

Taipei Veterans General Hospital (TVGH) is committed to digital transformation with the primary goal of enhancing the quality and safety of patient care, improving governance efficiency, and reducing clinical staff workload. In recent years, the hospital has made efforts in energy conservation and digital transformation to promote effective resource utilization and sustainability.

To achieve patient-centered digital transformation, TVGH comprehensively examines and develops smart healthcare from the patients' perspectives, including hospital referrals, outpatient services, emergency services, inpatient care, surgery, nursing, pharmaceuticals, diagnostic testing, medical administration, environmental maintenance, and post-care telemedicine and home care. In terms of technology, artificial intelligence plays a crucial role, along with technologies such as the Internet of Things, business intelligence, blockchain, cloud-based applications, big data analytics, telemedicine leveraging high-speed 5G transmission, 3D printing, augmented reality, and virtual reality. These technologies are not only widely applied in daily clinical practices but also serve as important tools for clinical training and advanced research. The latest supercomputer, "Veterans No. 1 Cloud," was launched in 2023 to support the hardware and computing power requirements of the aforementioned digital transformation.

In addition to pursuing large-scale cross-hospital projects with government agencies such as the National Science Council, the Ministry of Digital Development, and the Ministry of Health and Welfare, the hospital actively collaborates with domestic information and communication technology giants such as Microsoft Taiwan, ASUS, Quanta, Acer, Chunghwa Telecom, Advantech, and Philips. The hospital has been recognized with numerous domestic and international awards for smart healthcare innovation, including the 2024 Best Smart Hospital award by Newsweek.

The tighter integration of healthcare and information and communication technology is an international trend. TVGH must not hesitate or be content with the current situation at this critical moment. The combination of artificial intelligence and healthcare is highly anticipated and will likely be the decisive factor in the next phase. The hospital will mobilize its research and development team, recruit more colleagues and experts, and expand collaboration with relevant organizations domestically and internationally, including the neighboring Beitou Science Park. It aims to collaborate with biotechnology and information communication technology companies in the park, as well as nearby medical centers, medical universities, and research institutions to develop into a benchmark smart healthcare industry cluster in northern Taiwan.

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康健永續：CiC以創新科技解決全球面臨的重大健康福祉挑戰

Sustainable Wellness: CiC Addressing the Significant Global Health Challenges Through Innovative Technology

時 間：113年6月22日 08:30-16:30

Time：June 22, 2024 08:30-16:30

地 點：臺北榮民總醫院 醫學科技大樓一樓會議室

Place：TMedical Science and Technology Building
Taipei Veterans General Hospital

康健永續：CiC以創新科技解決全球面臨的重大健康福祉挑戰

Sustainable Wellness: CiC Addressing the Significant Global Health Challenges Through Innovative Technology

Tid1 innovations for nursing education practice in Houston Methodist

Tid1 利用創新來應變未來的護理教育跟照護

Hsin-Mei Chen

陳欣玫

Center for Nursing Research, Education and Practice, Houston Methodis Hospitalt, Houston, TX

Department of Nursing, Houston Methodist Academic Institute, Houston, TX

休斯頓衛理公會醫院

With the aging population increasing and medicine advancement, we will need more nurses, especially those who can handle complicated conditions and devices. As the nursing education department manager, I anticipate nurses needing more training. At the same time, it is tough to add more staff to the department. I will need to be more innovative in learning and creating learning lessons that can significantly improve nursing skill knowledge at the bedside, which leads to excellent clinical outcomes.

I worked with my collaborator to create the VR simulation of standardized physical assessment based on our previous two publications to show the benefit of the training. We have recruited nurses from our new-hire orientation since those will be naïve to the training. After consenting to the study, the participants are randomly assigned to 3 groups: traditional LMS, 2D VR, and 360 ˚ VR learning module. After the training, we analyzed their performance on skill validation and asked them to provide us with feedback on the simulation.

We have collected 249 n as of March 27, 2024. Nurses come across diverse backgrounds, specialties, and working experiences. In general, participants felt the VR simulation provided a more realistic experience, which is essential for them to learn the skill (Traditional LMS, 90%; 2D VR, 91%; and 360 ˚ VR, 97%). When validating their skills, the assessment completion rates are comparable (Traditional LMS, 98%; 2D VR, 97%; and 360 ˚ VR, 98%).

The three training groups use the same video footage, but VR provides the learners with different learning experiences with the same content. We are pleased to see the outcome. In addition to the convenience of using VR for future simulation training, VR also allows us to create more interactive content in the future. We plan to expand VR education and explore technology to create realistic simulated experiences for nurses in the hospital.

Modeling revolution and its significance in the consilience of humanities and science

我們與「人」的距離：介於人文與科學之間的「道路」

Shu-Heng Chen
陳樹衡
Department of Economics, National Chengchi University, Taipei, Taiwan, ROC
國立政治大學 經濟學系

Technology has the potential to significantly contribute to enhancing human health, extending lifespans, and fostering a sense of respect for life. However, despite these advancements, it is imperative to explore the underlying motivations behind these pursuits. Why do we inherently desire these improvements, especially if life were devoid of meaning? Would we prioritize a shorter yet more meaningful existence over a longer but potentially mechanized life? These questions naturally lend themselves to ethical and philosophical inquiries, highlighting the intrinsic connection between humanity and scientific progress.

In this discourse, we assert the indispensability of integrating humanities into the evaluation of technological progress. Merely advancing technology does not guarantee a meaningful life. Mary Shelley (1797-1851)'s classic novel, 'Frankenstein,' despite its age, remarkably foreshadowed contemporary ethical dilemmas. Biologist Edward Wilson (1929-2021), a proponent of interdisciplinary collaboration, advocated for the convergence of humanities and science. He followed in the footsteps of earlier pioneers such as Jonathan Swift (1667-1745), whose 'Battle of Books' in the late 17th century also emphasized this connection. Despite centuries of efforts, the fundamental divide between humanities and science persists.

In this discourse, we contend that the interdisciplinary cross between humanities and science faces significant hurdles, chiefly due to the inherent complexity of humanity, particularly its individuality. This individuality poses a formidable challenge to formal language in science, such as Newtonian mathematics or equation-based modeling (EBM). For instance, the intricate interactions among the more than five hundred protagonists in Leo Tolstoy (1828-1910)'s 'War and Peace' highlight the inadequacy of EBM in capturing the nuanced complexities of human behavior.

Approximately three decades ago, Nobel Laureate in Physics Murray Gell-Mann (1929-2019) introduced agent-based mathematics and modeling (ABM) as an alternative approach to tackling the complexities of human behavior. ABM not only enables us to navigate this intricate landscape but also capitalizes on recent advancements in information and communication technology (ICT) and artificial intelligence (AI), including technologies like ChatGPT. In conclusion, we emphasize that ABM is not only well-suited for modern technological applications but also serves as an effective bridge between the humanities and science.

How mathematical models are applied to consider the treatment of cancers

數學模型如何用來思考癌症治療

Jeng-Huei Chen
陳政輝
Department of Mathematical Sciences, National Chengchi University, Taipei, Taiwan, ROC
國立政治大學 應用數學系

Chemotherapy is widely used in the treatment of different cancers. However, resistance caused by the mutation of cancer cells reduces the efficacy of drugs and imposes great challenge to the treatment. To study the resistance problem, in 1979, Goldie and Coldman proposed the first stochastic-based model to relate the drug sensitivity of tumors to their mutation rates. Many scientists have since referred to this pioneering work because of its simplicity and elegance. Its original idea has also been extended and further investigated in massive follow-up studies of cancer modeling and optimal treatment. Goldie and Coldman, together with Guaduskas, later used their model to explain why an alternating non-cross-resistant chemotherapy is optimal with a simulation approach. Subsequently in 1983, Goldie and Coldman provided a rigorous mathematical proof to their earlier simulation work. However, their analytical study of optimal treatments majorly focused on a process with symmetrical parameter settings, and presented few theoretical results for asymmetrical settings.

In this talk, we first provide an introduction to Goldie and Coldman's model, which shows how probabilistic framework is used to describe the mutational behavior of cancer cells. Afterwards, we recast and restate Goldie, Coldman, and Guaduskas' model as a multi-stage optimization problem. With an asymmetrical assumption, the conditions under which a treatment policy can be optimal are derived. Numerical results are also presented to justify the correctness of the theoretical findings. If time permitted, we will also discuss some of our recent progress and related topics on this study. Instead of presenting all mathematical details, the focus of the talk is to demonstrate how mathematical models can be used in studying medical problems and to help clinical practitioners to re-think what are good treatment policies from different viewpoints.

From quantification and modeling to the automated generation of precision medical imaging

由量化 , 模型化 , 到自動生成的精準醫學影像

Chung-Ming Lo

羅崇銘

Graduate Institute of Library, Information and Archival Studies, National Chengchi University, Taipei, Taiwan, ROC

國立政治大學 圖書資訊與檔案學研究所

"Precision medical images from quantification, modeling to automatic generation" covers the complete process from image acquisition to diagnostic decision-making. As medical images become digitized, a critical next step is quantification, which is the extraction of measurable and precise data from radiological or pathological images. For example, radiomics through image processing technology can be used to obtain detailed information reflecting histological characteristics, which is crucial for lesion analysis and treatment planning.

Diverse quantitative features can be combined through artificial intelligence machine learning or deep learning to establish predictive models to assist diagnosis and treatment. Automatic segmentation and classification can mark and classify normal and abnormal tissues to achieve objectivity, consistency, high efficiency and high accuracy of interpretation.

AI-generated image reports help completely record the entire process. Automatically generated reports provide structured image analysis, including key pathological features and potential quantitative indicators. Embed clinical decision support in reports for faster condition assessment and subsequent treatment planning.

Precision medical imaging enhances the value of medical imaging and makes medical processes more intelligent and customized, thereby providing better patient care. The prognosis of malignant tumors and the assessment of blood vessel quality are used as examples to demonstrate the clinical practicality and feasibility of smart medicine.

Precision medicine and artificial intelligence

精準醫學與人工智慧

Chih-Hsun Wu

吳致勳

Interdisciplinary Artificial Intelligence Center, National Chengchi University, Taipei, Taiwan, ROC

國立政治大學 人工智慧跨域研究中心

Precision medicine refers to the careful assessment of disease heterogeneity and the separation of patients into different groups in order to develop strategies for disease diagnosis, prevention, and treatment. It is also known as P4 Precision Medicine, encompassing the four principles of Predictive, Preventive, Personalized, and Participatory.

Precision medicine and artificial intelligence (AI) have a close and intertwined relationship. Precision medicine emphasizes personalized healthcare, customizing treatment plans and therapies based on individual factors such as genetics, environment, and lifestyle. AI plays a crucial role in this process, leveraging big data analysis and machine learning/ deep learning techniques to help doctors identify patterns of diseases, predict disease progression, and provide personalized medical recommendations.

The rapid advancement of AI has made the realization of precision medicine more feasible and effective. At the same time, precision medicine provides valuable data and samples that serve as essential inputs for training and improving AI algorithms. This symbiotic relationship drives the continued progress and integration of precision medicine and AI in the medical field. For example, the development of non-invasive AI systems for multiple cancer prediction demonstrates how precision medicine and AI collaborate to advance personalized healthcare.

In summary, precision medicine and AI work closely together, jointly driving the growth of medical technology and providing patients with more accurate and personalized treatment options, while also equipping doctors with more powerful tools to address complex medical challenges.

The applications of microRNA in medicine

微型 RNA 在醫學的應用

Nianhan Ma

馬念涵

Department of Biomedical Sciences and Engineering, National Central University, Taoyuan, Taiwan, ROC

國立中央大學 生醫理工學院 生醫科學與工程學系

MicroRNAs (miRNAs) have diverse applications in medicine due to their ability to regulate gene expression post-transcriptionally. One key application is their use as biomarkers for disease diagnosis and prognosis, where specific miRNA expression patterns can indicate different disease states. In addition, miRNAs are being explored as therapeutic targets for various diseases. This presentation will demonstrate the several miRNA research as below.

Radiation is one of the main cancer therapies, however, radioresistance leading to recurrence and metastasis remains an unsolvable issue. In our study, miRNA expression in plasma from patients with head and neck cancer was related to radiotherapy. Our results indicated the miRNA enhanced the radiosensitivity of head and neck cancer cells through modulating ITGA5 and prevented radiation-induced bystander effects (RIBEs) activities via exosomes. This study showed a possible novel therapeutic strategy for head and neck cancer.

Long-term Peritoneal dialysis (PD) may cause peritoneal fibrosis. Encapsulating peritoneal sclerosis (EPS) is a rare, but fatal complication in long-term PD. We used a high-throughput real-time polymerase chain reaction (RT-PCR) arrays to screen for differentially expressed miRNAs of PD effluents from the patients with or without EPS. The receiver operating characteristic (ROC) curve analysis of the 5 miRNA-ratios combined with 2 clinical characteristics was shown to distinguish non-EPS and EPS of PD patients with 0.87-0.99 of area under the curve (AUC) in different analysis strategies. Our results indicate that EPS-associated miRNAs could prevent the mesothelial to mesenchymal transition and that miRNA expression profiles in the PD effluents could be an ancillary diagnosis tool for EPS in patients.

Smartphone-based artificial intelligence using a transfer learning algorithm for the detection and diagnosis of middle ear diseases

在智慧型手機中使用遷移學習算法診斷中耳疾病

Yen-Chi Chen, Yuan-Chia Chu, Albert C. Yang, Wen-Huei Liao, Yen-Fu Cheng

陳彥奇、朱原嘉、楊智傑、廖文輝、鄭彥甫

Department of Otolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital,Taipei ,Taiwan, ROC

Institute of Brain Science, National Yang Ming Chiao Tung University ,Taipei ,Taiwan, ROC

Kaohsiung Municipal Gangshan Hospital, Kaohsiung,Taiwan, ROC

(Outsourced by Show-Chwan Memorial Hospital)

國立陽明交通大學 腦科學研究所 及 臺北榮民總醫院 耳鼻喉頭頸醫學部 及 高雄市立岡山醫院

Background: Middle ear disorders pose common challenges for clinicians offering healthcare for pediatrics and teenagers, often leading to delayed or misdiagnosed cases. The integration of deep learning has the capability to enhance clinician support in identifying and diagnosing eardrum disorders through imaging.

Methods: Retrospectively, oto-endoscopic images were gathered from ologists at Taipei Veterans General Hospital between January 1st, 2011, and December 31st, 2019. Those collected images were de-identified and subjected to data pre-processing, augmentation, and splitting before being input into CNN training models. To address the complexity of middle ear disorders, 9 CNN-architectured models were developed for the recognition of these conditions. The most effective models were selected and combined into a compact CNN suitable for mobile phone deployment. The pretrained model was transformed into a smartphone-based application and assessed for its effectiveness in detecting and classifying 10 different middle ear ailments in accordance with oto-endoscopic images.

Results: Totally 2,820 clinical pictures of eardrums were utilized in the training of the model, resulting in the development of a program exhibiting high accuracy in detecting binary outcomes (pass/refer) within oto-endoscopic images, covering 10 distinct disease categories. Following model optimization, the accuracy reached an impressive 98.0%. The program showcased a seamless recognition process, featured a user-friendly interface, and revealed outstanding performance, achieving a classification accuracy of 97.6% across ten categories.

Conclusion: We have effectively created a deep learning model with the ability to identify and categorize eardrum ailments. The utilization of point-of-care diagnostic devices integrated with artificial intelligence-driven automated classification offers pragmatic solutions for real-world medical scenarios, particularly in the diagnosis of middle ear disorders and the implementation of telemedicine.

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消化系及甲狀腺手術之新趨勢

The State of the Art in Digestive and Thyroid Surgery

時　間：113年6月22日　08:30-12:00

Time：June 22, 2024　08:30-12:00

地　點：臺北榮民總醫院 中正樓10樓 一般外科會議室

Place：10F, The Conference Room, Chung Cheng Building
Taipei Veterans General Hospital

消化系及甲狀腺手術之新趨勢

The State of the Art in Digestive and Thyroid Surgery

Case sharing in multimodality treatment for locally-advanced pancreatic head cancer

局部晚期胰臟癌多型性治療經驗分享

Bor-Shiuan Shyr

石柏軒

Division of General Surgery, Department of Surgery and Therapeutic and Research Center of pancreatic Cancer, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 一般外科 及 胰臟癌治療暨研究中心

Background

Locally advanced pancreatic head cancer were considered as unresectable disease; however, with the adaptation of neoadjuvant treatment with advanced modern radiotherapy technique, more-and-more studies demonstrated promising outcomes of such patients after receiving conversion surgical treatment. We hereby present our humble experience of the first case of initially unresectable locally advanced pancreatic head cancer treated with conversion pancreaticoduodenectomy surgery after neoadjuvant chemotherapy and carbon-ion radiotherapy.

Presentation of case

A 74-year-old man was initially diagnosed with locally advanced pancreatic head-to-uncinate process ductal adenocarcinoma with tumor encasing SMV/main portal vein and obliteration of splenic artery, common hepatic artery, and SMA (cT4N0M0). After receiving 8 weeks of neoadjuvant chemotherapy Gemcitabine (1000mg/m2 on day 1, 8, and 15 in 4 weeks cycle) followed by 12 fractions of concurrent carbon-ion radiotherapy, a dramatic decline in serum tumor marker CA 19-9 from 219 U/mL to 50.4 U/mL was observed. He then underwent another 7 weeks of maintenance chemotherapy with SLOG regimen (oral S-1, leucovorin, oxaliplatin, and gemcitabine) followed by conversion pancreaticoduodenectomy surgery with successful R0 resection. Narrowing of portal vein with massive ascites and micro liver abscess were observed after surgery, which were successfully treated by percutaneous portal vein stenting and intravenous antibiotic therapy.

Conclusion

This is our first case experience of initially locally advanced unresectable pancreatic head cancer successfully treated with conversion surgery after neoadjuvant chemotherapy and carbon-ion radiotherapy.

The development and current trends of bariatric surgery

減重手術的發展及當前趨勢

Ching-Yun Kung

宮慶雲

Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 一般外科

For nearly two decades, bariatric surgery has stood as the cornerstone in treating morbid obesity, backed by compelling evidence from randomized controlled trials affirming its effectiveness and safety.

Currently, laparoscopic sleeve gastrectomy (LSG) is the most commonly performed bariatric surgery, followed by Roux-en-Y gastric bypass (RYGB). However, in the past 10 years, more and more treatment options have been emerging, including glucagon-like peptide-1 receptor agonist (GLP1-RA), endoscopic intervention and newly developed bariatric surgical procedures. The development of those new weapons for obesity makes it possible for us to provide personalized treatment according to the condition of each patient.

Hereby, the development of bariatric surgery will be introduced, and further trends will be discussed, with the goal of providing tailored treatment options for morbid obese patients.

Benefits and limitations of endoscopic thyroid surgery

內視鏡甲狀腺手術之優勢及限制

Hon-Fan Lai

黎瀚棻

Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 一般外科

Endoscopic thyroid surgery has revolutionized the field of thyroid surgery, offering patients an alternative to traditional open procedures. Two popular techniques, Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) and Bilateral Axillo-Breast Approach (BABA), have gained prominence for their efficacy and cosmetic outcomes. This review compares the benefits and limitations of TOETVA and BABA, highlighting their unique characteristics and considerations.

TOETVA is a scarless thyroidectomy technique performed through the oral vestibule, minimizing visible neck scarring. It offers excellent cosmetic outcomes, particularly appealing to young patients or those with cosmetic concerns. Despite its advantages, TOETVA is not suitable for all patients. The technique is limited to select cases with specific criteria, such as small thyroid nodules. Patients with a history of neck surgery or significant thyroiditis may also be poor candidates for TOETVA due to increased technical difficulty and risk of complications.

On the other hand, BABA is a bilateral axillo-breast approach that offers a more versatile approach to thyroidectomy. BABA provides excellent exposure of the superior pole of thyroid gland, allowing for safe dissection and precise identification of critical structures. However, BABA is not without limitations. The technique requires incisions in the axilla and breast, which may result in visible scars, although they are generally well-concealed. BABA also has a longer learning curve compared to TOETVA, requiring specialized training and experience to master.

In conclusion, both TOETVA and BABA offer distinct advantages and limitations in the field of endoscopic thyroid surgery. The choice between TOETVA and BABA depends on various factors, including patient suitability and surgical expertise. Further research and experience are needed to refine these techniques and optimize outcomes for patients undergoing endoscopic thyroid surgery.

Fluorescence imaging in liver surgery

螢光顯影於肝臟手術之應用

Shu-Cheng Chou

周書正

Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 一般外科

Intraoperative fluorescence imaging has become used widely for real-time visualization of biological structures and assessment of blood perfusion. In hepatobiliary surgery, fluorescence imaging using indocyanine green can be applied in the following applications.

Fluorescence cholangiography: fluorescence images of the extrahepatic bile ducts can be obtained by intrabiliary injection of ICG solution (0.025 mg/mL) or preoperative intravenous injection (IV) of ICG (2.5 mg). The latter technique begins to be used worldwide for confirmation of the bile duct

Identification of hepatic tumors: IV-injected ICG (0.5 mg/kg) accumulates in hepatocellular carcinoma tissues and in non-cancerous hepatic parenchyma surrounding liver metastasis, which can be used for intraoperative identification of subcapsular hepatic tumors by fluorescence imaging.

Hepatic segmentation: ICG solution (0.25 mg in 5 mL solution) is injected into a tumor-bearing portal branch under ultrasound guidance (positive staining technique). ICG can also be administered intravenously following closure of a corresponding portal pedicle (negative staining technique). These techniques enable long-lasting delineations of segmental boundaries throughout hepatectomy procedures because ICG retains in hepatocytes for more than 5 hours.

These techniques will develop into an indispensable intraoperative navigation tool, which may enhance accuracy of hepatobiliary surgery especially in the minimally invasive setting.

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大腸直腸癌手術的治療進展

Recent Trends and Advances in Surgery for Colorectal Cancer

時　間：113年6月22日　09:00-12:00
Time：June 22, 2024　09:00-12:00

地　點：臺北榮民總醫院 中正樓12樓(618胃腸科討論室)
Place：12F, The Conference Room 618, Chung Cheng Building
Taipei Veterans General Hospital

大腸直腸癌手術的治療進展

Recent Trends and Advances in Surgery for Colorectal Cancer

Use of machine learning to increase the detection of central lymph node metastasis in colon cancer

在大腸癌的患者中，以機器學習改善中央淋巴結轉移的偵測

張世慶

Shih-Ching Chang

Department of Surgery, Faculty of Medicine, National Yang-Ming Chiao Tung University, and Division of Colon & Rectal Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

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

Complete mesocolic excision (CME) with central vascular ligation (CVL), in which surgeons performed meticulous dissection in the mesocolic plane with ligation of the supplying vessel at its origin to remove all of the lymph nodes in the regional mesocolon proposed by Hohenberger could improve colon cancer patients ‘ outcome. The systematic review and meta-analysis found that patients operated on by CME had better disease-free survival. Disease-free survival in the CME/D3 group was statistically significantly different compared to the conventional group. The most important indication of CME is LN metastasis. Currently, the most commonly used and reliable assessment method is the evaluation of lymph nodes metastasis and tumor staging through enhanced computed tomography (CT). However, the complex grouping of the lymph nodes leads to technical difficulty in CT evaluation, and false-negative and false-positive (FP) results are inevitable. The accuracy of LN detection was around 50% and limited the indication of CME.

In recent years, steady progress has been made in deep learning technology. Artificial intelligence-assisted image recognition technology is currently able to detect the target area of an image and make classifications according to the detected target features, which is similar to the diagnosis process of the radiologist. This approach also represents a new solution for the above problems. Based on deep learning of medical imaging knowledge and network construction, the medical image artificial intelligence-assisted automatic recognition system, can identify specific lesions through the identification and labeling of lesions, with automatic volume delineation and three-dimensional reconstruction of target areas.

Since 2015, our lab collected 78 patients receiving curative colectomy. After elimination of personal and clinical data, we cooperated with deep learning engineer, Prof. Chang. After extraction of the quantitative CT image features, the patients were randomly separated into two groups by keeping the same distribution of the metastatic and normal LNs in training (80%) and test cohorts (%20). The training cohort consisted of 62 patients with 42 metastatic and 43 normal LNs while 16 patients with 11 metastatic and 12 normal LNs included in the test cohort.

In the clinical model, metastatic LNs were differentiated from normal LNs by evaluating the diameter of the LNs in the direction of the longest axis. 64.87% of the LNs were diagnosed correctly using clinical diagnostic criteria that correspond to correct classification of LNs. the model had an AUC of 0.704 (95% CI: 0.675, 0.733) for training and 0.772 (95% CI: 0.718, 0.825) for test cohorts. The radiomic-derived model demonstrated better performance for training (81.09%) and test cohorts (79.49%) in terms of accuracy with an increase of over 15% compared to the CT-image diagnostic criteria. Our results support that deep learning technology applying in imaging analysis could help the clinical physician to arrange surgical decision.

The benefit and indication of complete mesocolic excision

完整結腸繫膜切除之益處及適應症

Jin-Tung Liang

梁金銅

Division of Colorectal Surgery, Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan, ROC

臺大醫院 大腸直腸外科

Background/aim: To assess surgical outcomes of patients undergoing D3 lymph node dissection and complete mesocolic excision for the treatment of right-sided colon cancer in the context that both procedures were performed laparoscopically.

Methods: 244 consecutive patients with clinically staged III right-sided colon cancer were recruited to undergo the laparoscopic D3 lymph node dissection with complete mesocolic excision. Postoperatively, the patients were stratified as N0, N1, N2, and N3 groups according to the level of lymph node metastasis, prospectively followed up for more than 5 years, and compared.

Results: The 5-year cumulative recurrence rate and the estimated time-to-recurrence [mean (95 % confidence interval)] was 16.6 % (n = 7/42), 113.8 (101.4-126.2) months in N0 group; 21.3 % (n = 17/80), 108.9 (99.1-118.7) months in N1 group; 43.2 % (n = 32/74), 85.4 (73.0-97.8) months in N2 group; and 52.0 % (n = 25/48), 65.2 (49.0-81.4) months in N3 group. When N1 and N0 groups of patients were lumped together, and compared with patients with N2 or N3 metastasis, we found that the latter were with a significantly higher recurrence rate ($p < 0.0001$). D3 lymph node dissection with complete mesocolic excision could assure the harvest of sufficient number (n = 34.4 ± 8.4) of lymph nodes for precise pathologic cancer staging. Skip lymph node metastasis was detected in 19.8 % (n = 40/202) of patients, and such surgical procedures facilitated up-staging in 4.5 % (n = 11/244) of patients.

Conclusion: The present study encourages the dissemination of such concepts to surgical oncologists dealing with colorectal cancer through didactic education, and international consensus meeting is therefore mandatory to optimize the surgery of colon cancer.

The techniques and pitfalls of intracorporeal anastomosis in laparoscopic colectomy

腹內腸吻合之要點及盲點

Tzu-Liang Chen

陳自諒

China Medical University Hsinchu Hospital, and School of Medicine, China Medical University, Hsinchu, Taiwan, ROC

中國醫藥大學新竹附設醫院 及 中國醫藥大學 外科學科

Intracorporeal anastomosis, the creation of a surgical bowel connection within the abdominal cavity, has gained traction in laparoscopic colectomy procedures due to its potential advantages. However, this technique requires high technical proficiency and presents unique challenges that surgeons must navigate meticulously.

This presentation explores the intricate techniques involved in intracorporeal anastomosis and highlights the potential pitfalls at each procedural step. Key focus areas include:

Anastomotic techniques: This section provides an overview of various methods, such as stapled, hand-sewn, and compression anastomoses, detailing their advantages, limitations, and technical nuances.

Instrumentation and equipment: Exploration of specialized instruments like articulating staplers, endoscopic suturing devices, and anastomotic compression devices, including proper selection, handling, and troubleshooting strategies.

Exposure and visualization: Techniques for maximizing the surgical field, such as patient positioning, port placement, and ancillary device utilization, to achieve optimal exposure within the confined abdominal cavity.

Bowel mobilization and preparation: Strategies for meticulous bowel mobilization, vascular control, and bowel stump management as essential prerequisites for successful anastomosis.

Complication management: Potential complications like anastomotic leaks, strictures, bleeding, and intraoperative and postoperative management approaches.

This comprehensive presentation aims to give attendees a deep understanding of the technical nuances, instrumentation, and potential pitfalls associated with intracorporeal anastomosis in laparoscopic colectomy. By mastering these techniques and anticipating challenges, surgeons can enhance patient safety, minimize complications, and optimize outcomes in this technically demanding procedure.

Shaping the future of surgery with the da Vinci Robotic System: Updating evidence and looking beyond

達文西機械手臂手術之近期實證及未來展望

Chien-Chih Chen

陳建志

Department of Surgery, Koo Foundation Sun Yat-Sen Cancer Center Hospital, Taipei, Taiwan, ROC

醫療財團法人辜公亮基金會和信治癌中心醫院　外科部

In recent years, there has been significant progress in the development of robotic surgical system. In addition to well-known features such as wrist functionality, stereoscopic vision, and a stable working environment, robotic surgical system has become an integrated platform for various advanced technologies. These integrated advanced features will usher future surgical procedures into a realm that is safer for patients and more user-friendly for surgeons.

In the presentation, I will provide updates on the latest literature regarding robotic arms in the field of colorectal surgery, including comparative analyses of disease treatments and the impact on the surgical learning process for young surgeons. Additionally, I will introduce the characteristics of the latest generation of surgical robots and present new prospects for clinical practice.

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關節及肢體重建之新科技及趨勢

New Treading & Technology in Joint and Limb Reconstruction

時　間：113年6月22日　09:00-12:00

Time：June 22, 2024　09:00-12:00

地　點：臺北榮民總醫院 中正18樓骨科部會議室

Place：18F, The Conference Room , Chung Cheng Building
Taipei Veterans General Hospital

關節及肢體重建之新科技及趨勢
New Treading & Technology in Joint and Limb Reconstruction

Pedicle freezing by freezing tank for malignant bone tumors

惡性腫腫瘤之免截骨生物性重建

Po-Kuei Wu

吳博貴

Joint Reconstruction,Department of Orthropaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Therapeutical and Research Center of Musculoskeletal Tumor, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部 關節重建科

臺北榮民總醫院 骨科部 骨骼肌肉腫瘤治療研究中心

Background and Aim:Biological reconstruction of limbs affected by osteosarcoma is frequently assisted by liquid nitrogen cryoablation of resected tumor-bearing bones. In the present study, we have adopted an appropriately designed freezing tank with increased flexibility in positioning to assist pedicle-freezing. We aim to compare the peri-surgical improvements and complications between free-freezing and freezing tank-assisted pedicle freezing.

Methods:A retrospective review of our hospital database was conducted to screen for eligible patients (n=114) who received adjunctive limb salvage treatments for osteosarcoma during June 2017 to January 2019. After excluding patients who received treatments other than cryoablation and autograft biological reconstruction, a total of 41 patients had received free-freezing (n=20) or freezing tank-assisted pedicle freezing (n=21) were deemed eligible. Patient baseline demographics, oncological outcome, union rate and complications were compared between the free-freezing and the freezing tank-assisted pedicle-freezing groups.

Results:The number of osteotomies received was 1.55 per patient (31 osteotomies in 20 patients) in the free-freezing group, whereas it was 0.43 per patient (9 osteotomies in 21 patients) in the freezing tank-assisted pedicle-freezing group. The total number of graft-derived complications including soft tissue failure and structural failure were comparable between the two groups at 1 year after surgery. Three incidences of atrophic nonunion (9.7% of osteotomies) were observed in the free-freezing group, and none occurred in the freezing tank-assisted pedicle freezing group. Tumor progression and early infection occurred in 5% of patients treated by free freezing, and none was observed in those treated by freezing tank-assisted pedicle-freezing.

Conclusion:Freezing tank-assisted pedicle-freezing and free-freezing demonstrated comparable oncological outcome, but pedicle-freezing was associated with shorter time-to-union, lower non-union rate, an improved trend of osteotomy healing and functional recovery.

Osteoporosis influences the stem results of total hip replacement? Bone health optimization may play an important role

骨質疏鬆是否影響全人工髖關節術後骨柄的預後？骨骼健康優化或許扮演一個重要的腳色

Yu-Kuan Lin

林育寬

Joint Reconstruction, Department of Orthropaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部 關節重建科

The volume of total joint arthroplasty (TJA) procedures has risen in recent decades. On the basis of 2000 ~ 2014 data, the primary total hip replacement (THR) grows up to 71%, to 635,000 procedures on 2030.

The prevalence of osteoporosis in patients undergoing THR is up to 24.8%, and the prevalence is significantly higher in females (29%) than male. However, only 33% of them are treated for osteoporosis before surgery. The low bone marrow density (BMD) highly corresponds to associated complications after TJA, such as periprosthetic fracture, stem subsidence, and aseptic loosening. Aro HT, et al. mentions less BMD is associated to more stem subsidence. Lee SW, et al mentions osteoporosis decreases the osseointegration of the stem in THR, and it increases the risk of stem subsidence and stem loosening. Due to this, bone health optimization may play an important role for patient before TJA procedures. Anti-osteoporosis treatment prevents early periprosthetic bone loss after uncemented THA and lower all-cause mortality after fracture surgery comparing with patients who don't receive further treatment.

From anatomy to graft biomechanics and biology: Case studies in distal tibia biological reconstruction

遠端脛骨生物性重建，從解剖、植骨生物特性到生物力學

Kuan-Lin Chen

陳冠林

Joint Reconstruction, Department of Orthropaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部 關節重建科

Treating malignant bone sarcoma around the ankle presents significant challenges, with various techniques proposed for management. Reconstruction options include endoprosthesis or biological methods employing allograft or recycled autograft. This study focuses on the long-term follow-up and natural progression of biological reconstruction following wide excision for ankle bone sarcoma.

From 2004 to 2024, consecutive cases of biological reconstruction following wide excision for ankle bone sarcoma were included. A total of 33 patients were included, with a median follow-up duration of 120 months. All patients underwent wide excision, graft reconstruction (either autograft or recycled autograft), and syndesmotic fusion. Initial permanent ankle arthrodesis was performed in 15 cases, with plating-based fixation used in 28 cases and intramedullary nail in five cases. Oncological outcomes, functional status, and graft-related imaging findings were recorded.

Biological reconstruction following wide excision for bone sarcoma around the ankle proves to be a viable option. However, the optimal fixation strategy lacks direct comparison in long-term follow-up studies. This long-term report on the natural course of biological reconstruction around the ankle provides insight into fixation construct planning and future implant design.

Biological reconstruction for distal femur osteosarcoma: Different strategies for different age groups

依據年齡而制定的遠端骨肉瘤生物性重建

Pai-Han Wang

王柏涵

Joint Reconstruction, Department of Orthropaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部 關節重建科

Osteosarcoma usually occurs around the metaphysis of the distal femur or proximal tibia and needs wide excision with the adjacent joint and replacement by biological reconstruction or a megaprosthesis. An advantage of this surgery is that it maintains the adjacent joint and preserves the growth of the residual epiphysis, which provides excellent limb function. Various reconstruction options are available, including allograft, tumor-devitalized autograft, vascularized fibula graft, distraction osteogenesis, and custom-made implants.

Surgical strategy for biological reconstruction after tumor wide excision can be determined by the patient's age and the location of the tumor. Locations of extremity osteosarcomas. Patients with major invasion of tumor across the diaphysis were classified as "diaphysis". "Type I" denotes tumor border does not invade beyond the epiphyseal line or plate and is at least ≥1 cm from these structures; "Type II" denotes tumor is <1 cm from the epiphyseal line or plate ; and "Type III" denotes tumor is invading beyond the epiphyseal line or plate. Type I tumor may be managed by intercalary resection and preserves patient's growing potential. Bone prosthetic composite may contribute to good function and quality of life. However, leg length discrepancy is an issue when facing the younger age group. Osteconcondral reconstruction can be done by pedicle freezing and ligament reconstruction. Tumor recurrence and instability will occur in some percentage. Fusion is an old fashion done by allograft and trident fixation. Few cases survive well and still preserve acceptable leg length discrepancy.

Innovations in managing extra-articular deformity in primary total knee arthroplasty: A comprehensive approach

當膝關節置換手術遇到關節外畸形的不同處理策略

Chao-Ming Chen

陳昭銘

Joint Reconstruction, Department of Orthropaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部 關節重建科

Total knee arthroplasty (TKA) remains the gold standard for treating end-stage knee osteoarthritis and other degenerative joint diseases. However, the management of concomitant extra-articular deformities presents a unique set of challenges that require innovative approaches to ensure optimal outcomes for patients. Herein, we would like to review recent advancements in the management of extra-articular deformity during primary TKA, focusing on the integration of navigation, robotic surgery, personalized 3D printing jig design, computer simulation, and concomitant extra-articular osteotomy.

Navigation systems, including image-less and image-based systems, have revolutionized TKA by providing real-time feedback to surgeons, enabling precise implant positioning and alignment. In the context of extra-articular deformities, navigation assists in preoperative planning and intraoperative execution, facilitating the correction of complex alignment abnormalities while preserving bone stock and soft tissue integrity. Similarly, robotic-assisted surgery offers enhanced precision and accuracy, particularly in cases requiring intricate bone resections and ligament balancing to address extra-articular deformities. The combination of navigation and robotics represents a synergistic approach to achieving optimal implant positioning and alignment while minimizing intraoperative variability.

On the other hand, preoperative computer simulation and personalized 3D printing technology have emerged as a valuable tool in the management of extra-articular deformities, allowing for the creation of patient-specific cutting guides and jigs tailored to the individual anatomy of each patient. These custom-made instruments improve the accuracy of bone resections and facilitate the correction of deformities with greater precision and reproducibility. Furthermore, computer simulation enables virtual preoperative planning, allowing surgeons to visualize the desired correction and anticipate potential challenges before entering the operating room. This can be much helpful when performing concomitant extra-articular osteotomy in a single surgical session.

In conclusion, the management of extra-articular deformity in primary TKA requires a comprehensive and multidisciplinary approach, integrating the latest advancements in navigation, robotic surgery, personalized 3D printing jig design, computer simulation, and concomitant extra-articular osteotomy. By leveraging these technologies and techniques, surgeons can achieve optimal outcomes and improve the quality of life for patients with complex knee pathology.

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心領神會—核子醫學的心視野與退化性神經疾病研討

Joint Symposium on Nuclear Cardiology and Neurology Taiwan Society of Nuclear Medicine 2024

時　間：113年6月22日　08:00-17:00
Time：June 22, 2024　08:00-17:00

地　點：臺北榮民總醫院 第三門診9樓創意谷
Place：The Clinical Innovation Center,
Taipei Veterans General Hospital

心領神會—核子醫學的心視野與退化性神經疾病研討

Joint Symposium on Nuclear Cardiology and Neurology Taiwan Society of Nuclear Medicine 2024

The impact of AI-enhanced nuclear cardiology for accurate diagnosis and risk prediction

人工智慧對輔助核醫心臟影像診斷及預後判斷之效應

Yuka Otaki

Department of Radiology, Sakakibara Heart Institute, Tokyo, Japan

Currently, cardiologists have the benefits of multiple non-invasive cardiac imaging technologies including Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), a significant leap from what was available in previous years. The role of nuclear cardiology has evolved, now prioritizing the precise diagnosis of myocardial ischemia and the effective risk stratification for future cardiovascular events. To meet these objectives, expert readers are now increasingly utilizing software quantification tools alongside visual assessment to refine the diagnosis process. This approach not only enhances the accuracy of diagnoses but also streamlines the workflow within the nuclear cardiology lab. The integration of artificial intelligence (AI) into this process is posed to revolutionize the field further by optimizing imaging processing and significantly improving the precision of both diagnoses and prognoses derived from nuclear cardiology imaging.

In this presentation, the author delves into detailed insights and experience garnered over eight years in a cardiovascular imaging lab in the US. Through this exploration, the presentation aims to underscore the vital role and immense potential of nuclear cardiology in the contemporary era, characterized by the widespread adoption of multimodal imaging strategies.

Motion detection and correction: Are are we ready for clinical implementation?

影像位移及校正之臨床落地應用：我們是否已經做好準備？

Martin Lyngby Lassen
University Hospital Copenhagen Rigshospitalet, Denmark

Nuclear cardiology has advanced rapidly in recent years. One of the driving factors has been the increasing sensitivity, improved spatial resolution, and ingenuity in designing PET/CT, SPECT/(CT), and PET/MRI scanners. Consequential to the improved spatial resolutions (with resolutions of ≈ 1mm in latest generation PET/CT systems), even subtle motion during the acquisitions risks introducing detrimental blurring to the resulting images. For cardiac imaging protocols, motion during the scans can be divided into four distinct types: cardiac contractions, respiratory motion, patient motion, and myocardial creep. Unique motion detection and correction patterns have been devised for perfusion imaging protocols to minimize the impact of motion or even correct the motion. Detection of cardiac contractions is utilized in routine assessments, where it is often monitored using a 3-lead ECG device, while several techniques have been proposed to detect respiratory motion during the scans. The most common are respiratory bellows, infrared systems, and finally, data-driven methods.

Besides perfusion imaging, automated motion correction algorithms are also emerging for dynamic scans, thus facilitating the assessment of myocardial blood flow and flow reserves with motion-limited imaging series.

This presentation seeks to cover the current state-of-the-art in detecting and correcting for motion during cardiac PET and SPECT acquisitions.

Advances in nuclear imaging for the diagnosis of ATTR

ATTR 診斷相關核子影像醫學之進展

Christoph Rischpler
Klinikum Stuttgart, Germany

Cardiac amyloidosis (CA) is an underdetected cause for heart failure which has significantly gained attention in the past years. Systemic amyloidosis is a disorder that leads to extracellular deposition of misfolded proteins affecting organ function. In the vast majority of cases light-chain (AL) or transthyretin (ATTR) amyloid deposits are responsible for CA, leading to systolic and diastolic dysfunction, hypertrophy, arrhythmias, conduction blocks, and heart failure. Cardiac involvement is the most significant prognostic factor in patients with amyloidosis. AL amyloidosis can be treated with different anti-plasma cell regimens. In case of hematological response5 organ responses with improving organ function are possible. In ATTR amyloidosis disease specific therapeutic approaches include transthyretin stabilizers or transthyretin gene silencers.

The diagnosis of amyloidosis is based on Echocardiography, ECG, Laboratory Tests, Cardiac Biomarkers, Catherization, Magnetic Resonance Imaging, and Nuclear Imaging but a reliable diagnosis is provided only by histopathological examination. Nuclear imaging plays an important role in diagnosis and monitoring of illness.

Until recently endomyocardial biopsy has been the “gold standard” for diagnosing all types of cardiac amyloidosis, but non-invasive strategies are emerging. It has been known for few years now that accumulation of bone-seeking radiopharmaceuticals like 99 m Tc-3 , 3-diphosphono-1 , 2-propanodicarboxylic acid (99mTc-DPD) have very high accuracy in diagnosing ATTR amyloidosis.

Positron-emission tomography with computed tomography (PET-CT) has also been explored as a diagnostic tool for cardiac amyloidosis and recent studies have shown the promise of 18F-flutemetamol PET imaging for detecting ATTR cardiac amyloidosis.

In the speech we will address the advances in nuclear imaging as regards to the diagnosis and confirmation of ATTR.

Hereditary ATTR: A neurological perspective

從神經內科學的角度探討遺傳型 ATTR

Sung-Tsang Hsieh
謝松蒼
Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan, ROC
臺大醫院 神經部

Hereditary transthyretin (ATTR) amyloidosis is characterized by a slowly progressive peripheral sensorimotor and/or autonomic neuropathy as well as non-neuropathic changes of cardiomyopathy, nephropathy, vitreous opacities, and CNS amyloidosis. Neurological involvement usually starts in the lower extremities with paresthesias and hypesthesias of the feet, followed within a few years by motor neuropathy. In some persons, particularly those with early-onset disease, autonomic neuropathy is the first manifestation of the condition; findings can include: orthostatic hypotension, constipation alternating with diarrhea, attacks of nausea and vomiting, delayed gastric emptying, sexual impotence, anhidrosis, and urinary retention or incontinence. Cardiac amyloidosis is mainly characterized by progressive cardiomyopathy. Individuals with leptomeningeal amyloidosis may have the following CNS findings: dementia, psychosis, visual impairment, headache, seizures, motor paresis, ataxia, myelopathy, hydrocephalus, or intracranial hemorrhage.

Disease onset typically occurs in adult life, with age and presenting symptoms largely depending on genotype. Initial signs usually include pain, temperature sensation loss, numbness or tingling in lower limbs extremities. Motor neuropathy progressively ensues causing walking instability, inability to walk unassisted and ultimately need for a wheelchair. Autonomic symptoms, including bowel abnormalities, early satiety, orthostatic hypotension and erectile dysfunction may appear in the initial stages of the disease, particularly in patients with an early onset phenotype. Heart involvement, with signs of infiltrative cardiomyopathy leading to heart failure, develops in the majority of patients. Most patients are therefore classified as mixed phenotype (both neurological and cardiac). With respect to drug prescription, impairment due to polyneuropathy is scored with the familial amyloidotic polyneuropathy (FAP) staging system which has three stages : stage 1 is defined by unassisted walking; stage 2 is defined by need for assisted walking and stage 3 is defined by wheelchair-bound or bedridden patient.

Amyloid-PET image quantification

類澱粉蛋白正子掃描圖像量化

Norman Koglin

Head, Scientific Operations (Clinical R&D) at Life Molecular Imaging, Germany

Background : Amyloid positron emission tomography (PET) with [18F]florbetaben is an established tool for detecting Aβ deposition in the brain in vivo and has been approved for routine clinical use since 2014 as Neuraceq® based on visual assessment (VA) of PET scans. Quantitative measures are however commonly used in the research context, with many of the available PET software packages capable of calculating amyloid burden both on a regional and a composite level, allowing continuous measurement of amyloid burden in addition to the approved dichotomous VA.

Methods : This study aimed to provide scientific evidence of the robustness and additional value of florbetaben PET quantification, with a focus on Centiloid-based analysis. The diagnostic performance (i.e., sensitivity and specificity) of quantification against the histopathological confirmation of Aβ load was estimated and compared to the effectiveness of the approved VA method. Additionally, the concordance between visual and quantitative evaluation of florbetaben PET scans was assessed. The reliability and comparability of the different analytical pipelines was further tested. Florbetaben PET images analyzed in this retrospective analysis had been acquired in previous clinical trials. The study population consisted of 589 subjects with at least one available florbetaben PET scan. Florbetaben PET scans were quantified with 15 analytical pipelines using nine software packages that used several metrics to estimate Aβ load (SUVR, Centiloid, amyloid load and amyloid index). Six analytical methods reported Centiloid.

Results : The mean sensitivity, specificity, and accuracy were 96.1 ± 1.6%, 96.9 ± 1.0%, and 96.4 ± 1.1%, respectively, for all quantitative methods tested when compared to histopathology, where available. The mean percentage of agreement between binary quantitative assessment across all 15 methods and visual majority assessment was 92.4 ± 1.5%. Assessments of reliability, correlation analyses, and comparisons across software packages showed excellent performance and consistent results between analytical methods.

Conclusion : This study demonstrated that quantitative methods using both CE marked software and other widely available processing tools provided comparable results to visual assessments of FBB PET scans. Software quantification methods, such as centiloid analysis, can complement visual assessment of FBB PET images and could be used in the future for identification of early amyloid deposition, monitoring disease progression and treatment effectiveness. Based on this study, quantification of [18F]florbetaben PET as an adjunct to visual assessment was recently approved by the European Medicines Agency (EMA) in the EU for Neuraceq®.

Evolving PET tracers in neurological disorders

神經疾病中不斷發展的 PET 示蹤劑

Matthias Brendel

Professorship for Translational Molecular Imaging, Germany

This lecture will provide an overview of the current use of new PET tracers in preclinical and clinical research and the latest understanding of biomarkers in neurological disorders. Three topics will be presented in more detail: (i) Advances in Tau PET research for AD and movement disorder patients, (ii) A new approach for ATN assessment, (iii) Cell sorting after radiotracer injection to decipher the PET signal source.

Advances in Tau-PET research for AD and movement disorder patients: Tau-PET emerged as a valuable biomarker for the differentiation of the 4-repeat (4R) tauopathy progressive supranuclear palsy (PSP) from healthy and disease controls. Furthermore, we applied a novel approach of cell sorting after radiotracer injection and observed higher tracer uptake in single neurons compared to astrocytes of PS19 mice. Regional [18F]PI-2620 tau-PET signals in vivo correlated strongly with abundance of fibrillary tau in subsequent autopsy samples of PSP patients and disease controls. In an additional autopsy sample of deceased patients with PSP, tau-positive neurons with high AT8 density but not tau-positive astrocytes were the driver of [18F]PI-2620 autoradiography signals. In summary, neuronal tau constitutes the dominant signal source of tau-PET signal increases in 4R-tauopathies, yielding the capacity to translate to an in vivo signal.

ATN assessment using kinetic modelling of a single Tau-PET session : Patients with neurodegenerative

diseases are classified molecularly using the A/T/N classification system. Apart from fluid biomarkers and structural MRI, the A/T/N system utilizes characteristic features from Amyloid-PET (A), Tau-PET (T), and FDG-PET (N), requiring multiple imaging sessions. Thus, we evaluated the value of dynamic tau-PET with [18F]PI-2620 to assess A/T/N in individual patients during a single imaging session. Perfusion [18F] PI-2620 images (R1) were validated as a surrogate marker for neuronal injury, exhibiting strong quantitative and visual correlations with early-phase Amyloid-PET and FDG-PET, as well as with volumetric MRI and CSF total tau levels. Our results suggest that [18F]PI-2620 imaging has the potential to facilitate the assessment of PET-based A/T/N during a single dynamic PET session.

Cell sorting after radiotracer injection deciphers the PET signal source: Various cellular sources hamper interpretation of positron-emission-tomography(PET) biomarkers in the tumor microenvironment (TME). Combining cellular tracer uptake measures with 3D-histology facilitates precise allocation of PET signals and serves to validate emerging novel TAM-specific radioligands.

Taiwanese nuclear medicine brain image database: From construction to research application

台灣核子醫學腦影像資料庫：從建置到研究運用

Yu-Ching Ni
倪于晴
National Atomic Research Institute, Department of Radiation Protection , Taoyuan, Taiwan, ROC
國家原子能科技研究院 輻射防護研究所

Through collaboration between the National Atomic Research Institute's Radiation Imaging Group and the domestic medical community, a nuclear medicine cerebral blood flow imaging database specifically designed for the Taiwanese population has been established. This presentation will introduce the progress of the database construction, the composition of the dataset, and its scale. Additionally, it will share the results of dementia differentiation research conducted using this database, with the hope of enhancing the diagnostic capabilities for dementia and the application value in related research fields in the future.

International non-invasive atherosclerosis imaging-review and prospect

非侵入性動脈粥狀硬化造影的研發現況與應用

Chien-Chung Hsia
夏建忠
National Atomic Research Institute, Department of Isotope Applications, Taoyuan, Taiwan, ROC
國家原子能科技研究院 同位素應用研究所

Chronic inflammation of arteries due to hyperlipidemia leads to thickening and loss of elasticity of the arterial wall connective tissue, resulting in atherosclerotic lesions. In the mechanism of vascular inflammation, macrophages play a key role. There are now many radiopharmaceuticals in imaging atherosclerosis. Among them, the chemokine C-X-C receptor type 4 (CXCR4) plays an extremely important role in inflammation and tumor biology. A new small molecule antagonizing CXCR4 was designed through computer simulation technology. The chemical structure of the agent APD was verified by radioisotope labeling and effectiveness in the ApoE-/- mouse model. The results represent that 68Ga-APD can be rapidly excreted through the kidneys and can be found in the atherosclerotic lesions of ApoE-/- mice/ The background ratio (TBR) is >10 (0.5~1.5 hours after drug injection), and the sensitivity and specificity are better than existing related drugs in the world. This imaging technology platform has been successfully used in clinical medicine and healthy food efficacy Through verification, the research and development cycle of new cardiovascular-related drugs and healthy foods will be further shortened in the future, and research and development costs and failure risks will be significantly reduced.

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精準麻醉與永續醫療：術後加速康復療程(ERAS)的創新與進展

Precision Anesthesia and Sustainable Healthcare: Innovations and Advances in Enhanced Recovery After Surgery (ERAS)

時　間：113年6月22日　08:30-12:00
Time：June 22, 2024　08:30-12:00

地　點：臺北榮民總醫院 第三門診9樓創新沙龍
Place：The Clinical Innovation Center,
Taipei Veterans General Hospital

精準麻醉與永續醫療：術後加速康復療程(ERAS)的創新與進展

Precision Anesthesia and Sustainable Healthcare: Innovations and Advances in Enhanced Recovery After Surgery (ERAS)

Enhanced recovery for liver recipient: What we do for perioperative care

加強術後恢復在肝臟移植受贈者經驗分享

Shen-Chih Wang

王審之

Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 麻醉部

Considering the dramatic hemodynamic changes during liver transplant, liver recipients are vulnerable to organ damage. The challenge to improve quality of liver recipients' recovery is how to integrate what we already know into practice. The general principles we followed for liver transplant perioperative care are:

1. Adequate hydration: We use beat to beat stroke volume variation derived from arterial blood pressure waveform to guide our isotonic crystalloid hydration.
2. Adequate perfusion pressure: We try our best to keep the mean blood pressure above 65mmHg. However, surgical procedures dealing with shunting due to portal hypertension vary case by case.
3. Avoid unnecessary anesthetic agents use: We use BIS index to guide our anesthetic agents use and surgical pleth index to guide our opioid use during the surgical procedure.
4. Avoid unnecessary blood product use: After years of experience in TEG-guided transfusion strategy, we now transfuse our patient only for uncontrollable bleeding.
5. Avoid postoperative opioid use: We use bilateral rectus sheath catheters for local anesthetic wound infiltration after liver transplant. Our result indicates that this is an effective and uncomplicated way to decrease postoperative opioid use.

Comorbidities of liver recipients sometimes make these general principles difficult to follow. To further individualize perioperative care for every liver recipient, we investigate the information hidden beneath the arterial blood pressure waveform. With unsupervised manifold learning and diffusion map, we analyze the morphology dynamics of arterial blood pressure waveform. Currently we are able to show that richer variation of arterial waveform correlates to better outcomes. Such correlation cannot be explained by blood pressure read outs. Our finding may provide a potential way toward delicate hemodynamic management to each liver recipient.

The making of a Spine ERAS Cocktail

脊椎 ERAS 麻醉雞尾酒

Jing-Yang Liou
劉靖楊
Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan ROC
臺北榮民總醫院 麻醉部

ERAS, as an emerging clinical pathway, is being increasingly implemented in many hospitals worldwide. Taiwan has just begun its pace in the long run. There's no hard definition to qualify for the term, but rather it represents a general direction for improving patient recovery. Stepwise component inclusion is often the case. One important anesthesia component is to provide precise general anesthesia that gives rapid and stable induction, maintainence and emergence. As more and more emphasis is laid upon recovery, one would easily work toward an opiod-sparing regime. Other drugs must be used to work around opioids, many of which may impact the clinical judgement of anesthesia precision. However, these drugs are in no way new or novel. The use of the non-opioid drugs in a perioperative and total intravenous anesthesia setting is discussed, including benefits and controversies whirlwinding around some of these drugs. We will share how our protocol has evolved through a 4-year journey of ERAS in spine surgery.

Application of precise anesthesia in breast surgery

精準麻醉在乳房手術中的應用

Wei-Nung Teng
鄧惟濃
Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 麻醉部

Breast surgery can be done with peripheral nerve blockade and intravenous sedation, which can reduce the side effects of general anesthesia such as nausea and vomiting, intubation discomfort and postoperative pain. The distribution of breast nerves is complex. Common nerve block methods are paravertebral blocks and pectoral nerve blocks. By using advanced monitors, the precise areas of analgesia may be confirmed. The analgesia nociception index and surgical plethmographic index are two important monitors in anesthesia. By monitoring the patient's heart rate change and measuring the patient's parasympathetic tone, the analgesic drug can be administered according to the patient's individual differences to avoid insufficient or excessive analgesic dose. The EEG derived density spectral array is another tool used in breast surgeries to help understand analgesia and sedation levels. Intraoperative and emergence DSA pattern may be used to predict post-operative pain and delirium.

From evidence-based medicine to digital twin

從實證醫學到數位雙胞胎

Li-Sheng Chen
陳立昇
College of Oral Medicine, Taipei Medical University, Taipei, Taiwan, ROC
臺北醫學大學 口腔醫學院

The evolution of healthcare science has seen significant advancements from Evidence-based Health in 1970, with clinical randomized intervention assessments, to Precision Health in 1990, which refined personal strategy models, and most recently to Smart Health in 2015, which incorporates Artificial Intelligence for real-time evaluations. To develop Smart Health, the real-time assessment of both physical and virtual health care information while maintaining the spirit of classical evidence-based health science is essential.

Anesthesia is a crucial component of patient care during surgery. Achieving the optimal depth of anesthesia tailored to individual patients and specific surgeries underscores the importance of precision personalized anesthesia. With technological advancements and the development of AI, precision personalized anesthesia has seen significant breakthroughs. The need for personalized monitoring in anesthesia includes the collection of big data and personal health information through electronic medical records and the Internet of Things to enable proactive deployment. Furthermore, the use of digital twins for precise anesthesia allows for better assessment and implementation, as well as post-operative rehabilitation.

This presentation will focus on the principal digital twins in the metaverse, discussing how to integrate personalized, precision machine learning models and incorporate federal learning to develop a new paradigm in metaverse healthcare.

The evolution of pain management in colorectal surgery: VGHTPE ERAS protocol

大腸直腸手術精準麻醉的演進：臺北榮總 ERAS 經驗

Yi-Shiuan Li
李易軒
Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 麻醉科

The Enhanced Recovery After Surgery (ERAS) Society care pathways include evidence-based items designed to reduce perioperative stress, maintain postoperative physiological function and accelerate recovery after surgery. Since the first published guidelines in 2005, providing a multimodal stress-minimizing approach has been shown repeatedly to reduce rates of morbidity, improve recovery and shorten length of stay (LOS) after major colorectal surgery.

The benefit of using a multimodal approach to pain management is based on the concept that several multiple pain reducing mechanisms will improve pain control while avoiding the side effects of each drug. Opioid avoiding or sparing techniques in colorectal surgery is associated with early mobilization, fast return of bowel function, fewer complications and a reduction in length of stay.

Enhanced recovery after pancreatic surgery in VGHTPE

胰臟手術後加速復健：臺北榮總經驗

Hui-Hsuan Ke

柯惠瑄

Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 麻醉部

Pancreatic surgery is a high-risk abdominal procedure with significant rates of complications and mortality. Advances in diagnostic and surgical techniques over recent decades, coupled with improvements in intensive care unit management, have led to better outcomes following pancreatic resections.

Enhanced Recovery After Surgery (ERAS) protocols represent perioperative care aimed at promoting early recovery postoperatively through strategies such as maintaining intravenous fluid restriction, early oral intake postoperatively, more effective pain management, early removal of drains and tubes, and early mobilization of patients. The goal of ERAS is to accelerate postoperative recovery and reduce length of hospital stay (LOS) without increasing morbidity or readmission rates.

Basic elements of ERAS protocols for pancreatic surgery include preoperative counseling, avoidance of mechanical bowel preparation, multimodal postoperative pain control, restrictive intravenous fluid therapy postoperatively, early oral feeding, early removal of nasogastric tubes, urinary catheters, and abdominal drains. Experiences at Taipei Veterans General Hospital demonstrate that implementing ERAS protocols for pancreatic surgery results in patients experiencing the aforementioned benefits, accelerating time to ambulation, increasing rehabilitation walking distance, and achieving higher patient satisfaction.

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急重症醫學之智慧醫療新進展

Smart Healthcare Advancements in Emergency and Critical Care Medicine

共同主辦單位：國立陽明交通大學急重症醫學研究所、
臺北榮民總醫院新生兒醫療中心、重症醫學部、
急診醫學部、胸腔外科、感染科、心胸麻醉科

時　間：113年6月22日　8:40-12:30
Time：June 22, 2024　8:40-12:30

地　點：臺北榮民總醫院　長青樓一樓會議室
Place：Nursing Arts Laboratory, Evergreen Building, Taipei Veterans General Hospital

急重症醫學之智慧醫療新進展

Smart Healthcare Advancements in Emergency and Critical Care Medicine

Double SMART ICU 2030

2030 機智加護中心

Huey-Wen Yien

尹彙文

Medical Artificial Intelligence Development Center, Surgical ICU, Taipei Veteran General Hospital, Taipei, Taiwan, ROC.

臺北榮民總醫院 醫療人工智慧發展中心 外科加護中心

In the era of digital transformation, the concept of "ICU without wall" can fix the unmet demand during the critically-ill patient journey which includes both critical and concierge care for the patients and families.

We propose the new model of critical care by AIR(AI and Robotics) to transform the delivery of continuity and comprehensive care in the paradigm shift of digital generation. The term of "**Double SMART**" represents both physical and digital dimensions, that is "**S**ervice, **M**anagement, **A**rchitecture, **R**esearch, **T**echnology" and "**S**afe/save, **M**obile, **AI**, **R**obotics, **T**rust/touch". We design a high performance process to de-load the low-value care, especially while facing the challenge of burnout and shortage of ICU staffs.

In Mercy Virtue hospital, the world's first facility dedicated to telehealth, they propose the "**Hospital without beds**" project. Physician staffs can "see" patients where they are. Another example is the "Journey with ***Guided Care***" in Cleveland Clinic Medical Center showing their great core value, "Every patient deserves world-class care. "

In conclusion, we are facing the great challenges in our traditional model of delivering low value care during patient journey including burnout of staffs, shortage of workforce, and finally collapse of the non-resilient medical care system. We are now on the AIR way to double SMART ICU 2030.

From concept to commercialization: The comprehensive journey of developing an ICU acute kidney injury prediction model

從概念到商業化：加護病房急性腎損傷預測模型的全方位發展之旅

Chun-Te Huang

黃俊德

Nephrology and Critical Care Medicine, Department of Internal Medicine and Critical Care Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 內科部 腎臟科 重症部 重症內科

Acute Kidney Injury (AKI) is a critical concern in ICUs, with a 30% prevalence and severe long-term consequences. Addressing this, our collaborative effort with Tunghai University and Advantech Technology led to a pioneering predictive model for AKI, forecasting incidents 24 hours in advance with remarkable accuracy. Through external validations at four medical centers and enhancements via federated learning, our model has been patented in Taiwan and the USA, and certified as a software medical device by Taiwan's FDA in December 2023. We are now moving towards clinical trials, aiming for broader clinical implementation and inclusion in Taiwan's National Health Insurance. This journey from concept to potential commercialization embodies a significant leap in ICU patient care, showcasing the power of collaboration, innovation, and perseverance in tackling healthcare challenges

From prediction to action: Sharing from CCM of Taipei VGH

從預測到行動：臺北榮總重症醫學部的分享

Dung-Hung Chiang

江東鴻

Department of Critical Care Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC.

臺北榮民總醫院 重症醫學部

"Prediction AI" refers to artificial intelligence systems that utilize machine learning, statistical analysis, and data mining techniques to predict future events, trends, or outcomes. Such AI systems predict future developments by analyzing past and present data, learning the patterns and correlations within.

"Actionable AI" refers to artificial intelligence systems capable of directly supporting decision-making and concrete actions. These AI systems go beyond mere data analysis or prediction; they provide specific recommendations, solutions, and can even autonomously execute particular tasks.

In recent years, the Department of Critical Care Medicine at Taipei Veterans General Hospital has also been committed to the development of intelligent critical care medicine. This presentation will introduce the department's achievements in developing prediction models and the progress towards implementing actionable AI.

Time matters: The application of AI in the critical care and trauma imaging

分秒必爭：外傷重症影像智能化判讀應用

Chi-Tung Cheng

鄭啟桐

Department of Trauma and Emergency Surgery, Chang Gung Memorial Hospital, Linkou Chang Gung University, Taoyuan, Taiwan, ROC

林口長庚紀念醫院 外傷急症外科

Trauma constitutes a critical medical scenario that often poses an immediate threat to life, necessitating rapid intervention to secure patient survival and the swift identification of affected organs. Physicians operating within such a high-stakes environment are tasked with the rapid assimilation and interpretation of a voluminous array of information and imaging, all within stringent time constraints. The efficacy of deep learning technologies has been substantiated across a spectrum of medical imaging domains, encompassing the identification of hemorrhages in brain CT scans, the detection of fractures in chest and pelvic X-rays, and the recognition of fluid in ultrasonography.

At the Trauma Department of Linkou Chang Gung Memorial Hospital, our aim is to harness deep learning algorithms across a diverse range of critical trauma imaging modalities, thereby advancing the development of a sophisticated computer-aided diagnosis (CAD) system. Our team has achieved notable success in formulating models for the detection of pelvic fractures in X-rays, the identification of rib fractures in chest X-rays, and the delineation of spleen injuries in abdominal computed tomography scans.

Looking forward, our ambition is to seamlessly integrate this CAD system within the existing clinical information system and to incorporate these models into the trauma imaging alert system. This integration is envisioned to furnish an automated diagnostic support for critical injuries in trauma patients across multiple healthcare facilities. By enabling the early diagnosis of severe injuries, our initiative stands to significantly enhance the caliber of trauma care, thereby preserving patient lives and optimizing recovery outcomes.

Anesthesia department information system improvement, experiences of VGH Taipei

臺北榮總麻醉部資訊系統改良經驗談

Fu-Wei SU
蘇府蔚
Department of Anesthesiology,Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 麻醉部

Taipei Veterans General Hospital ranks as the twelfth largest hospital in the world by bed capacity. The high complexity in operating room management necessitates a process to reduce errors, maximize efficiency, and alleviate healthcare worker burnout. This preoperative preparation process for surgical patients involves coordination among multiple personnel and patients themselves.

Anesthesia evaluation begins at the early stage of preoperative preparation. We tried to develop an evaluation platform and use artificial intelligence to reduce the workload of anesthesiologists, to facilitate OR schedule management, and to reduce perioperative complications.

Experience sharing of critical care research and future directions in smart ICU

重症研究經驗分享及未來智慧加護病房研究方向

Wei-Chih Chen

陳威志

Department Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 胸腔部

陽明交通大學 醫學系

Critical care research is paramount in advancing our understanding of critical care medicine and facilitating enhanced patient care within the intensive care unit (ICU). The evolution of new technologies and electronic medical records has streamlined data collection processes for researchers, enabling them to acquire more data efficiently compared to previous methods. However, effectively harnessing the vast amounts of data generated by various ICU machines for precise analysis remains a significant challenge.

My research journey began during my residency, where I started at the process of topic exploration, securing institutional review board approval, designing case report forms, transitioning from hard copy to electronic database, utilizing statistical software for analysis, crafting figures and tables, manuscript composition, reference management, English editing, and the submission and revision process, including handling rejections.

The vision of a ‘smart ICU’ holds promise for revolutionizing clinical studies by offering unparalleled convenience. Additionally, establishing a nationwide network of ICUs holds immense potential for uncovering clinically significant insights that may not be apparent within single-center studies. In the current insurance system, hospital administrations are not willing to invest in ICU improvements due to less reimbursement from daily clinical care. However, the advancement of the ‘smart ICU’ is intrinsically tied to overall quality enhancement and improved patient outcomes. Hence, policymakers within governmental and hospital administration boards must allocate more resources and provide ample encouragement to ICU professionals to facilitate this progress.

Development and validation of a machine learning model for predicting the vascular access flow threshold in end-stage renal disease patients during hemodialysis

預測血液透析期間血管通路流量閾值：發展與驗證一個機器學習模型

Fan-Yu Chen
陳範宇
Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 腎臟科

Taiwan currently faces the highest global incidence and prevalence rates of end-stage renal disease (ESRD). The number of dialysis cases has risen significantly from 10,179 in 2010 to 12,346 in 2018, reflecting a 28.9% increase in individuals undergoing dialysis treatment, which escalated from 65,610 to 84,615 patients over the same period. Effective vascular access is imperative for the well-being and longevity of hemodialysis (HD) patients. Both the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Vascular Access and European guidelines advocate for arteriovenous fistula (AVF) as the preferred form of permanent vascular access for HD patients. Despite previous research indicating higher survival rates among AVF users compared to those with arteriovenous grafts (AVG) or central venous catheters (CVC), AVF may encounter functional decline and reduced blood flow over time due to vascular remodeling-associated inflammatory changes. These alterations often lead to stenosis, subsequent thrombosis, and eventual AVF failure, significantly impacting patient survival, morbidity, and quality of life. The KDOQI guidelines also stress that individuals with AVF access flow (Qa) <500 ml/min, AVG Qa <600 ml/min, or a 25% decrease in Qa over 3 to 6 months face heightened risks of stenosis or thrombosis. However, conventional measurement techniques like Doppler ultrasound and magnetic resonance angiography are operator-dependent, costly, and susceptible to errors. Taipei Veterans General Hospital, a leading medical institution in Taiwan, relies on the HD03 hemodialysis monitor (Transonic®) for quantitative hemodialysis surveillance, measuring Qa every three months during sessions. This monitor employs the ultrasound dilution method, also known as the Krivitski method, which involves injecting a saline bolus to measure intra-access flow rates. Nevertheless, many ESRD patients in Taiwan receive HD treatment at local clinics, where access to the HD03 monitor for routine Qa evaluation may be limited. To address this, our study utilizes an artificial intelligence-driven machine learning approach, leveraging routinely collected data, to predict occurrences of Qa <500 ml/min events for AVF during hemodialysis. By developing and validating a machine learning-based risk model, our research aims to facilitate personalized surveillance strategies, enabling risk stratification without burdening healthcare professionals further.

Smart wireless monitoring for infants

嬰兒智慧監測系統

Chia-Sui Chou

周佳穗

Neonatal Medical Care Center and Section of Neonatology, Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 兒童醫學部 新生兒醫療中心

Over the years, the government has continuously promoted baby-friendly hospitals, including implementing rooming-in for mothers and infants. During rooming-in, newborns stay with their mothers in postpartum wards without constant medical supervision nearby. This raises concerns about the timely detection of unstable vital signs in newborns. Using this smart wireless monitoring system for rooming-in newborns allows for real-time remote monitoring of their vital signs, enhancing the level of medical service and safety of hospitalized newborns.

The system is applied in the postpartum wards and baby rooms of Taipei Veterans General Hospital, utilizing devices approved by the Ministry of Health and Welfare. These devices monitor the newborns' blood oxygen saturation level, heart rates, and body temperatures, with the data collected and transmitted in real-time via 4G/5G networks to the monitoring platform. The data is displayed on medical station computer screens, enabling healthcare providers to constantly monitor the newborns' physiological conditions.

After implementing this system, newborns' vital signs can be monitored at any time and uploaded to the monitoring platform via the internet. This allows families in postpartum wards to be informed about the newborns' vital signs, while other healthcare personnel can remotely grasp the situation of rooming-in newborns, significantly reducing the pressure on healthcare providers and families, improving newborn safety, and enhancing the level of medical service and family satisfaction.

Using the smart wireless monitoring system for infant ensures the safety and health of rooming-in newborns, improves the quality of medical care, and addresses concerns about healthcare providers' inability to constantly visually monitor them.

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慶祝臺灣腹膜透析治療四十年：
歷史見證與未來展望

Celebrating 40 Years of Peritoneal Dialysis in Taiwan: Historical Testimony and Prospective Development

時　間：113年6月22日　08:30-12:00
Time：June 22, 2024　08:30-12:00

地　點：臺北榮民總醫院　重粒子中心會議室
Place：Heavy Ion Therapy Center,
Taipei Veterans General Hospital

慶祝臺灣腹膜透析治療四十年：歷史見證與未來展望

Celebrating 40 Years of Peritoneal Dialysis in Taiwan: Historical Testimony and Prospective Developmen

Improving technique survival and extending ToT: Strategy to better manage patients on PD

提升技術存活率與延長 PD 療程：更有效管理患者的策略

Allen Liu Yan Lun

Khoo Teck Puat Hospital (KTPH), Singapore

邱德拔醫院

Technique failure in peritoneal dialysis (PD), characterised by the necessity to switch from PD to haemodialysis or due to mortality, is a critical concern affecting patient outcomes. The presentation delineates insights for different duration-based definitions, which offer evidence to the likelihood of returning to PD post-failure.

The presentation discusses early technique failures, including infections, mechanical issues with catheters, and psychosocial factors. Mechanical causes, due to their reversible nature, show a higher probability of return to PD.

Risk factors for technique failure are scrutinised, revealing critical elements like prior renal replacement therapy, demographic influences such as age and race, and clinical settings, including centre size and patient management strategies. Moreover, several preventive strategies aim to reduce the incidence of technique failure, emphasising the importance of tailored treatment approaches and the specialised management of complications like catheter dysfunction and infections.

In conclusion, this presentation illuminates the complexities surrounding technique failure in PD and provides a comprehensive overview of how to effectively manage and potentially reduce these failures through strategic interventions and patient-centric care.

Sonography in peritoneal dialysis

超音波在腹膜透析的應用

Jenq-Wen Huang

黃政文

Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital , Taipei, Taiwan, ROC

臺大醫院 內科部 腎臟科

Ultrasound is a convenient examination tool with no risk of radiation exposure, and it can be readily performed by clinicians. In the context of complications in peritoneal dialysis (PD), there are many aspects where ultrasound can be utilized. For exit site infections, it can detect fluid accumulation around the external cuff, serving as an index for severity evaluation and a tracking indicator for treatment effectiveness. Fluid collection around the subcutaneous catheter can also confirm evidence of tunnel infection which could not be diagnosed solely by clinical inspection of the skin overlying the catheter sometimes. Fluid accumulation around the internal cuff confirms that the infection has affected the vicinity of the peritoneum, greatly increasing the chances of peritonitis which might need urgent catheter removal. Ultrasound can easily distinguish between hernias and leaks. Hernias keep intact peritoneum and contain a sac of fluid. On the other hand, leaks have peritoneal tear and soft tissue edema. In encapsulating peritoneal sclerosis (EPS), ultrasound can visualize calcification of the peritoneum, peritoneal thickening, loculated ascites, fibrin septum, gastrointestinal motility, and whether encapsulation has occurred. Therefore, ultrasound is a convenient, safe, and effective diagnostic and therapeutic monitoring tool in the management of complications in PD.

Since the detecting depth is shallow, less than 1 cm for catheter and cuff and less than 4 cm for the bowel loops, high frequency probe, around 7-12 GHz, should be used. In addition, dialysate or ascites serves as a good interface between parietal peritoneum lining on abdominal wall and visceral peritoneum wrapping the bowel loops.

The role of peritoneal dialysis in cardiorenal syndrome

腹膜透析在心腎症候群的角色

Ben-Chung Cheng

鄭本忠

Department of Nephrology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ROC

高雄長庚紀念醫院 腎臟科

This lecture examines the role of peritoneal dialysis in cardiorenal syndrome, a complex condition characterized by the interplay between heart and kidney dysfunction commonly seen in heart failure patients. Peritoneal dialysis, as a therapeutic modality, aids in alleviating symptoms and slowing the progression of cardiorenal syndrome by removing excess fluid and metabolic waste from the body. The lecture discusses the application, efficacy, comparative analysis with other treatment modalities, and future research directions of peritoneal dialysis in the management of cardiorenal syndrome. Through a comprehensive exploration of the role of peritoneal dialysis in cardiorenal syndrome, we aim to enhance understanding and management of this intricate condition, ultimately improving patients' quality of life and prognosis.

Sharesource: A tool with tremendous potential for the physician

Sharesource : 一個對醫生具有巨大潛力的工具

Karumathil Murali
Wollongong Hospital, Australia
澳大利亞 臥龍崗醫院

Peritoneal dialysis (PD) programs worldwide have integrated cloud-based remote monitoring tools such as Sharesource® into automated PD delivery. Sharesource® has become a ubiquitous tool within PD nurses' daily workflows, offering near-real-time monitoring of crucial PD parameters. Its utilization enhances patient-provider engagement, enables early detection of problems, and facilitates timely interventions, potentially reducing hospitalizations and enhancing PD outcomes. While physicians currently utilize Sharesource® to a much lesser extent than nurses, its significant potential not only lies in providing comprehensive insights into PD efficacy, adherence, and catheter function but aids in the evaluation of PD complexities. The rich data collected and presented by Sharesource® serves as a valuable resource for understanding and troubleshooting PD complications in conjunction with other clinical information, which is demonstrated by real-life examples. Sharesource Analytics® offers insightful trends derived from pooled data, aiding clinicians in navigating the complex treatment paths of PD patients, particularly in challenging clinical scenarios.

Hybrid method for PD catheter insertion

混合式腹膜透析導管植入術

Szu-Yuan Li

黎思源

Divisin of Nephrology, Deppart of Medicine Taipei Veterans General Hospital, Taipei, Taiwan, ROC

National Yang-Ming Chiao Tung University School of Medicine, Taipei, Taiwan, ROC

國立陽明交通大學 及 臺北榮民總醫院 腎臟科

Background: Peritoneal Dialysis (PD) stands as a cornerstone in treating end-stage kidney disease (ESKD), offering patients various methods for catheter insertion, each with its own set of pros and cons. The existing techniques include open surgery, laparoscopy, and percutaneous placement, chosen based on individual patient needs and medical history. Exploring innovative approaches to PD catheter insertion holds promise for expediting recovery and reducing complications, thus enhancing PD care quality. Researching novel methods of PD catheter insertion to expedite recovery and decrease the probability of complications may enhance the quality of PD care.We here reported a hybrid method of PD catheter insertion, which combines laparoscopic and percutaneous placement.

Methods: This retrospective study included patients who were undergoing their first PD catheter insertion, and a total of 20% of the enrolled patients had a past medical history of abdominal surgery. Out of these, one group of patients underwent the laparoscopic method, and another group underwent a new invented hybrid method. The study aimed to compare the surgical outcomes, incidence of early and late complications, hospital stay, and medical expenses between the two groups.

Results: There were no notable differences in basic demographic features and comorbid conditions between the two groups. The results of our data revealed that the hybrid group had a significantly shorter break-in period and did not require temporary hemodialysis. Additionally, length of hospital stay and medical costs were significantly lower in the hybrid group. The incidence of early complications was lower in the hybrid group, while the incidence of late complications was comparable between the two groups.

Conclusion: The hybrid method of PD catheter insertion provides a safe and efficient alternative to the traditional laparoscopic method, enabling urgent-start PD and reducing hospital stays and medical expenses. Our findings support the use of the hybrid method as a new standard of care for ESKD patients undergoing PD catheter insertion.

Peritoneal dialysis care experience at Taichung Veterans General Hospital

腹膜透析在臺中榮總的照顧經驗

Mu-Chi Chung

鍾牧圻

Division of Nephrology, Depart of medicine, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 腎臟科

This review delves into Taichung Veterans General Hospital's (TVGH) pioneering efforts in peritoneal dialysis (PD) care, emphasizing its contributions to research and innovative patient management strategies. TVGH's research has significantly advanced our understanding of hypokalemia and PD peritonitis, guiding targeted interventions to improve patient outcomes. The hospital's multidisciplinary team collaborates on translational studies, bridging the gap between bench and bedside to inform clinical practice.

Central to TVGH's approach is the implementation of a cloud management system tailored for PD patients. This technology enables real-time monitoring of vital signs and treatment adherence, facilitating early detection and intervention for complications such as PD peritonitis. By harnessing data analytics and remote monitoring, TVGH enhances efficiency and efficacy in patient care delivery.

Moreover, TVGH prioritizes patient-centered care, tailoring treatment plans to individual needs and fostering collaboration between patients and clinicians. Through shared decision-making and holistic support, TVGH empowers patients to actively participate in their treatment journey, ultimately enhancing their quality of life.

In summary, this review highlights TVGH's commitment to excellence, innovation, and patient-centered care in PD management. By advancing research, leveraging technology, and promoting collaborative care, TVGH sets a standard of excellence in nephrology, continually striving to optimize patient outcomes and redefine the future of renal care.

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遠距醫療數位轉型與永續發展

The Intersection of Homehospital and Sustainable Development Goals

時　間：113年6月22日　13:30-17:30

Time：June 22, 2024　13:30-17:30

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

遠距醫療數位轉型與永續發展

The Intersection of Homehospital and Sustainable Development Goals

As the wave of artificial intelligence sweeps in, where do our openings await?

人工智慧浪潮來襲，我們的機會在哪裡？

I-Chin Tu
杜奕瑾
Founder, Taiwan AI Labs
臺灣人工智慧實驗室

Large Language Models (LLMs) play a transformative role in healthcare by enhancing medical knowledge, supporting patient care, and optimizing communication. By leveraging vast datasets and deep learning techniques, LLMs can comprehend, summarize, and create medical content, thereby aiding in medical education and decision-making processes. Taiwan AI labs is pioneering the global AI landscape through its unique trustworthy AI evaluation system. By leveraging these endeavors, we now present FedGPT that is the foremost federated healthcare solution to enable a broad spectrum of applications in the hospitals. FedGPT empowers a smart medical system by integrating vast arrays of electronic health records (EHRs), medical images, genomic data, and clinical guidelines. Our discourse will focus on FedGPT's transformative functions, including its capacity for converting speech into structured documentation, augmenting diagnostic accuracy with multimodal AI, and ensuring compliance and disease coding. With accumulated efforts on understandings of over 37 million biomedical literature, we further leverage LLMs to strengthen disease prevention and health education efforts. More importantly, FedGPT applies federated technologies that can redefine data utility via open access to foster breakthroughs in personalized medicine research and healthcare operation efficiency. We invite you to join us in exploring the revolutionary impact of FedGPT as a new era of intelligent healthcare solutions.

Seamless healthcare: Integrating wearable devices and artificial intelligence to provide continuous patient monitoring

無縫醫療：整合穿戴裝置與人工智慧打造連續病患監護

Shih-Lin Chang

張世霖

Director of Healthcare and Services Center, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 健康管理中心

AIOT (Artificial Intelligence of Things) in telehealthcare refers to the integration of artificial intelligence (AI) and Internet of Things (IoT) technologies in the field of telehealth. Telehealthcare combines telecommunication and healthcare to provide remote diagnosis, monitoring, and treatment to patients, enabling healthcare professionals to deliver care from a distance. AIOT in telehealthcare of cardiac arrhythmia brings several advantages and opportunities: remote patient monitoring, predictive analytics, virtual consultations and diagnosis, treatment optimization, telemedicine robotics, data security and privacy.

While AIOT in telehealthcare of cardiac arrhythmia offers numerous benefits, challenges exist. These include ensuring interoperability between different IoT devices, addressing concerns about data privacy and security, integrating AI algorithms seamlessly into existing healthcare workflows, and maintaining ethical use of AI to avoid biases and ensure transparency in decision-making. AIOT has a potential to transform telehealthcare by enhancing patient care, improving diagnosis accuracy, enabling remote monitoring, and optimizing treatment strategies.

AI-Led cardiac electrophysiology: New perspectives from electrocardiograms to intracardiac electrograms arrhythmias

由 AI 引領的心臟電生理學：從心電圖到心內電圖的心律不整新視野

Men-Tzung Lo

羅孟宗

Department of Biomedical Science and Engineering

國立中央大學 生醫科學與工程學系

Atrial fibrillation (AF) isn't always triggered by a completely random process. Stable and rapid re-entrant circuits, leading to fibrillatory conduction throughout the atria, can persist for minutes, or even hours. Ablation targeted at the center of stable rotating waves and focal sources has shown a high rate of acute AF termination and improved long-term recurrence-free probability. However, in mapping the atrial substrate electrograms of AF, a common challenge is identifying culprit sites and analyzing wave propagation, especially for electrogram signals with significant temporal and spatial disparities. Localizing AF drivers using conventional sequential temporal-spatial mapping in persistent AF is even more challenging due to the lack of specificity of complex atrial electrograms, intermittent firing, and spatial meandering.

In my presentation, I will introduce newly developed systems featuring a multiple channels amplifier frontend, compatible with various types of catheters, and capable of achieving optimal computing efficiency for real-time ultra-high density mapping of atrial substrates through heterogeneous computation. These systems have the ability to interpret complex wave propagation and identify the substrate maintaining AF through Artificial Intelligence, thereby aiding in uncovering the true AF driver hidden beneath highly fragmented waves. My presentation will systematically compare automated electrogram analysis using real-time ultra-high density substrate mapping. This comparison aims to facilitate a better understanding of why these approaches enable instantaneous and objective identification of abnormal potentials accurately indicating AF drivers. It is noteworthy that these methods not only reduce the ablation area but also improve the acute termination rate and recurrence-free survival of AF.

ECG AI prediction system

心電圖 AI 診斷系統

Chih-Min Liu

劉至民

Heart Rhythm Center, Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 心臟內科 心律不整中心

The prevalence of pulmonary hypertension is approximately 1%, affecting over 25 million patients globally. Among these, those with pulmonary pressures exceeding 50mmHg face a five-year mortality rate greater than 30%. Early detection and treatment to prevent deterioration are essential. However, early symptoms are often overlooked, and the lack of accurate screening tools delays treatment, thereby increasing the risk of mortality. This issue is global, and the FDA has included one pulmonary pressure detection system in its Breakthrough Devices Program to accelerate its development.

The Pulmonary Hypertension Detection system (PHD) is an AI-assisted diagnostic ECG software designed for screening pulmonary hypertension. It is the first system of its kind to undergo multinational and multi-center international testing, including in Taipei and Taichung Veterans General Hospitals, National Cheng Kung University Hospital in Taiwan, and Makiminato Central and Nakagami Hospitals in Japan. The AI has demonstrated stable validation results, allowing rapid screening and providing diagnostic probabilities for pulmonary hypertension, thus aiding physicians in diagnosis. The diagnostic accuracy of this software is nearly three times greater than that of traditional ECG interpretations by physicians, significantly enhancing early diagnosis rates. The system has been internationally published and patented. The PHD system can be widely applied in hospitals, clinics, and health screening centers, requiring only a simple personal computer setup with ECG equipment to perform screenings, and provides results within 5-10 minutes. It can also operate remotely, enabling transnational ECG analysis. Currently, it is being industrially applied in collaboration with companies and has applied for TFDA approval as a medical device software.

CAD AI prediction system

冠狀動脈 AI 預測系統

Wei-Chieh Huang
黃偉杰
Division of Cardiology Department of Internal Medicine Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 心臟內科

Leveraging patient data through machine learning techniques in disease care offers a multitude of substantial benefits. Nonetheless, the inherent nature of patient data poses several challenges. Prevalent cases amass substantial longitudinal data owing to their patient volume and consistent follow-up, however, longitudinal laboratory data are renowned for their irregularity, temporality, absenteeism, and sparsity; In contrast, recruitment for rare or specific cases is often constrained due to their limited patient size and episodic observations. This study employed self-supervised learning (SSL) to pretrain a generalized laboratory progress (GLP) model that captures the overall progression of six common laboratory markers in prevalent cardiovascular cases, with the intention of transferring this knowledge to aid in the detection of specific cardiovascular event.

GLP implemented a two-stage training approach, leveraging the information embedded within interpolated data and amplify the performance of SSL. After GLP pretraining, it is transferred for target vessel revascularization (TVR) detection.The proposed two-stage training improved the performance of pure SSL, and the transferability of GLP exhibited distinctiveness. After GLP processing, the classification exhibited a notable enhancement, with averaged accuracy rising from 0.63 to 0.90. All evaluated metrics demonstrated substantial superiority ([Formula: see text]) compared to prior GLP processing. Our study effectively engages in translational engineering by transferring patient progression of cardiovascular laboratory parameters from one patient group to another, transcending the limitations of data availability. The transferability of disease progression optimized the strategies of examinations and treatments, and improves patient prognosis while using commonly available laboratory parameters. The potential for expanding this approach to encompass other diseases holds great promise. Our study effectively transposes patient progression from one cohort to another, surpassing the constraints of episodic observation. The transferability of disease progression contributed to cardiovascular event assessment.

Keywords: Cardiovascular diseases; cardiometabolic disease; disease progression; laboratory examinations; pre-train model; representation learning; self-supervised learning; time-series data; transfer learning.

AI enabled ECG signal system to predict CV event

AI 輔助生理訊號預測不良事件之發生

Ting-Yung Chang
張珽詠
Heart Rhythm Center, Division of Cardiology, Department of Internal medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 內科部 心臟內科 心律不整中心

Atrial fibrillation (AF), the most common arrhythmia in clinical practice, carries the potential for blood stasis and increased likelihood of thrombus formation, resulting in a higher risk of stroke and thromboembolism. The prevalence of AF is projected to be 4% in 2050, while the lifetime risk is approximately 1 in 7 for subjects aged ≥20 years. AF increases the risk of ischemic stroke, dementia, heart failure, myocardial infarction, and mortality. However, screeningof AF remains challenging, and underdiagnosis is commonin patients with paroxysmal AF (pAF) due to their highprevalence of asymptomatic AF. Subclinical AF is one of thepathogeneses of embolic stroke of an undetermined source(ESUS). Thus, early detection of occult AF is of paramount importance, in order to improve patient management. Timely diagnosis allows the implementation of appropriate interventions, either pharmacological or interventional, in order to prevent adverse effects, reducing morbidity and mortality. Implantable loop recorders have drawbacks, since their cost may hinder their implementation in certain healthcare systems. Moreover, adverse events, such as skin erosion, infections, device oversensing or undersensing can limit their effectiveness.Traditional methods of arrhythmia screening, such as electrocardiography (ECG) and continuous ambulatory Holter monitoring are mainly hampered by the limited period of rhythm recordings.

To increase the diagnostic rate of ECG monitoring and its cost-effectiveness, it is necessary to choose a patient who is expected to have AF. Artificial intelligence might be useful to predict adverse events, such as paroxysmal AF or VT in patients who showed sinus rhythm during 24-h Holter monitoring.The results of application of AI in digital heath should be interpreted very carefully to avoid possible bias and must be tested in RCTs.The combination of wearables with telemedicine might also lead to a revolution in community care, as well as a reduction in both acute hospital admission and health spending.

Intelligent pharmacist: AI assistant in telemedicine

智能藥師：遠距醫療的 AI 助理

Ju-Chieh Wung

翁如潔

Pharmacy department, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 藥學部

The COVID-19 pandemic has accelerated the integration of telemedicine as a standard healthcare service model. Traditional face-to-face interactions between medical professionals and patients have transitioned to those on digital screens, providing the foundation for the development of a diverse array of AI-powered medical tools, with a particular focus on image reading.

Our project focuses on image reading for prescriptions, which are displayed on video screens by patients during telemedicine consultations. Drug names are extracted using optical character recognition technology and converted into unique identification codes, such as international drug codes or medication license numbers, by referencing government open data sources. These identification codes undergo another round of matching with the patients' drug records from national health insurance or healthcare units, resulting in the automatic generation of intelligent pharmacist service documents. These documents offer support to medical personnel in delivering clinical pharmacy care.

This system is built upon well-established technologies, minimizing both development costs and time-to-market, while efficiently utilizing government open data resources to reduce expenses associated with database maintenance. By integrating AI-assisted clinical pharmacy services, our system effectively reduces pharmacist workloads, minimizes medication wastage, and decreases the risk of potential adverse drug events, ultimately enhancing the overall quality of healthcare delivery. This innovative approach not only optimizes healthcare processes but also upgrades patient safety and satisfaction within the evolving landscape of telemedicine.

Genetic predictors for atrial fibrillation related stroke

心房顫動相關之血栓性中風的全基因組關聯性研究

Chia-Ti Tsai

蔡佳醍

Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ROC

國立臺灣大學 醫學院 內科

Atrial fibrillation (AF) is a common cardiac arrhythmia and is one of the major causes of ischemic stroke. In addition to the clinical factors such as CHADS2 or CHADS2-VASC score, the impact of genetic factors on the risk of thromboembolic stroke in patients with AF has been largely unknown. Single-nucleotide polymorphisms (SNPs) in several genomic regions have been found to be associated with AF susceptibility. However, whether SNPs in other genomic regions are associated with AF-related thromboembolic stroke are unknown. Therefore, we hypothesize that in addition to CHADS2 or CHADS2-VASC score, genetic factor(s) may help identify AF patients with a higher risk of thromboembolic stroke. We propose a three years' project to conduct a genome-wide association study (GWAS) using whole genome sequence (WGS) data to identify these genetic factors. In the first and second years, we plan to consecutively recruit AF patients and perform WGS-based subgroup GWAS to identify new genes or loci related to thromboembolic stroke. In the second and third year, we will establish zebrafish, mouse, cellular and induced pluripotent stem cell (iPSC) models to provide a platform for drug testing and investigate the molecular mechanism by which the identified novel genes contribute to AF-related thromboembolic stroke. Our three-year's project is the first genome-wide WGS SNP study for AF-related thromboembolic stroke and will provide new genetic screen factors to help identify AF patients at risk of thromboembolic stroke and develop novel treatment strategy other than oral anticoagulants.

Endothelial progenitor cell in treatment of cardiovascular disease

內皮前驅幹細胞（EPC）治療心臟血管疾病的進展

Po-Hsun Huang

黃柏勳

Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Division of Cardiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

國立陽明交通大學 臨床醫學研究所

臺北榮民總醫院 心臟內科

Abstract

The last decade has shown considerable interest in regenerative biology, with particular emphasis on the use of isolated or purified stem and progenitor cells to restore structure and function to damaged organs. Circulating endothelial progenitor cells (EPC) were first discovered in 1997 by Dr. Asahara et al. who identified in the adult human peripheral blood a population of CD34 or kinase insert domain receptor (KDR)-positive cells and have been identified as a potential cell source that contributes to neovascularization via postnatal vasculogenesis. This notion challenged the previous concept that de novo formation of new blood vessels occurs only in the yolk sac mesoderm during embryonic development. Additionally, it is known that the integrity and functional activity of the endothelial monolayer play an essential role in atherogenesis. A series of clinical and basic studies have provided new evidence that the injured endothelial monolayer is regenerated by circulating EPCs. Circulating EPC number has also been reported to inversely correlate with the presence of risk factors of coronary artery disease. A better understanding of the relation between EPCs and atherosclerosis, and how EPC could provide treatment for cardiovascular disease, would provide additional insight into the pathogenesis of cardiovascular diseases and create novel therapeutic strategies.

Cardiac regeneration research using human pluripotent stem cell-derived cardiomyocytes

人類多能性幹細胞衍生的心肌細胞於心臟再生研究的進展

Yu-Feng Hu
胡瑜峰
Division of Cardiology, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 心臟內科

Electrical impulses from cardiac pacemaker cardiomyocytes initiate cardiac contraction and blood pumping and maintain life. Abnormal electrical impulses bring patients with low heart rates to cardiac arrest. The current therapy is to implant electronic devices to generate backup electricity. Instead, cardiac biological pacing has been developed as a hardware-free alternative. The approaches to generating biological pacing have evolved recently using cell reprogramming technology to create human pacemaker cardiomyocytes in-vivo or in-vitro. The reprogramming-based biological pacing recapitulates various phenotypes of de novo pacemaker cardiomyocytes and is more physiological, efficient, and easy for clinical implementation.

Development and validation of echocardiography-based machine-learning models to predict mortality

運用心臟超音波的機器學習模型預測死亡率

Chung-Lieh Hung

洪崇烈

Division of Cardiology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei, Taiwan, ROC

Institute of Biomedical Sciences, MacKay Medical College, New Taipei City, Taiwan, ROC

臺北市馬偕紀念醫院 內科 心臟科

馬偕醫學院 生物醫學科學研究所

Echocardiography remains a useful tool to evaluate heart function in patients with cardiac anomaly, especially for HF. Prior studies showed that cardiac systolic function evaluated by echocardiography is a strong prognosticator for HFrEF. However, burden of cardiac functional evaluation and potential bias by manual assessment remains limited. Echocardiography (echo) based machine learning (ML) models may be useful in identifying patients at high-risk of all-cause mortality. Herein, we introduced the clinical application and development of AI in echocardiography for automatic assessment of cardiac functions of HF irrespective clinical phenotypes. Additionally, ML models (ResNet deep learning using echo videos and CatBoost gradient boosting using echo measurements) was used to predict 1-year, 3-year, and 5-year mortality among HF patients from multi-center dataset. Models were trained on the Mackay dataset, Taiwan (6083 echos, 3626 patients) and validated in the Alberta HEART dataset, Canada (997 echos, 595 patients). We examined the performance of the models overall, and in subgroups (healthy controls, at risk of heart failure (HF), HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF)). We compared the models' performance to the MAGGIC risk score, and examined the correlation between the models' predicted probability of all-cause mortality. The ResNet and CatBoost models achieved area under the receiveroperating curve (AUROC) between 85% and 92% in internal validation. In external validation, the AUROCs for the ResNet (82%, 82%, and 78%) were significantly better than CatBoost (78%, 73%, and 75%), for 1-, 3- and 5-year mortality prediction respectively, with better or comparable performance to the MAGGIC score. ResNet models predicted higher probability of death in the HFpEF and HFrEF (30%–50%) subgroups than in controls and at risk patients (5%–20%). We concluded that Echo-based ML models are practical and useful to predict mortality showed good internal and external validity and were generalizable and are comparable to an established HF risk score. These models can be leveraged for automated risk stratification at point-of-care (POC) as perspectives.

Disclosure

(Funding)

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Application of AI in cardiovascular disease

應用人工智慧深度學習於心血管疾病與個體化差異關聯性研究

Ping-Yen Liu
劉秉彥
Institute of Clinical Medicine, National Cheng Kung University, Tainan, Taiwan, ROC
Chair of Medicine, Division of Cardiology, Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan,ROC
成大醫院 內科部
成功大學 醫學院 臨床醫學研究所

Background: How to identify high-risk population for next-generation drug-eluting stent (DES) with instent restenosis (ISR) by genetic studies has not been investigated. We thus aimed to study the power of genetic risk score to identify high-risk population for next-generation DES with ISR.

Methods and Results: We enrolled coronary artery disease patients receiving next-generation DESs from January 2010 to December 2019 in our hospital. The participants were classified into the derivation cohort and validation cohort to determine genetic risk score of next-generation DES with ISR. The genetic risk score was defined as the sum of the number of selected exonic single nucleotide polymorphisms (SNPs) for the risk allele. There were 2,749 patients receiving next-generation DESs and 205 patients having DES with ISR confirmed by coronary angiography. Six hundred thirty patients (age: 64.4 ± 10.1 years, male: 80%) were included for genotyping analysis: 72 patients had DES with ISR. After propensity score matching, there were 343 patients and 153 patients in the derivation and validation cohorts, respectively. Five selected SNPs, i.e., SNPs in *CAMLG, GALNT2, C11orf84, THOC5, and SAMD11*, were included to calculate the genetic risk score for next-generation DES with ISR. In the derivation cohort, patients with a score ³3 had significantly higher DES with ISR rates (hazard ratio [HR]: 5.17, 95% confidence interval [CI]: 2.57–10.38, $p < 0.001$). In the validation cohort, the prevalence of DES with ISR in patients with a score ³3 was also significantly higher than that in patients with a score <3 (HR: 3.68, 95% CI: 1.37–9.86, $p < 0.001$).

Conclusion: We demonstrated the significant association between the five SNPs-derived genetic risk score and DES with ISR. This model could provide incremental biological information for interventional cardiologists prior to percutaneous coronary intervention.

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抗風濕病藥物的角色－從基礎研究到臨床應用的過程

Role of Anti - Rheumatic Medication-From Basic to Clinic

時　間：113年6月22日　13:30-17:30

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

抗風濕病藥物的角色－從基礎研究到臨床應用的過程

Role of Anti - Rheumatic Medication- From Basic to Clinic

Evolution of rheumatoid arthritis, past, now and future

進化中的類風濕性關節炎，未來還有哪些可能性？

Fu-Chiang Yeh

葉富強

Department of Rheumatology , Immunology and Allergy, Tri-Service General Hospital, Taipei, Taiwan, ROC

三軍總醫院 過敏免疫風濕科

Rheumatoid arthritis (RA), an evolving autoimmune disease, profoundly affects joint function. Its complex pathogenesis remains under constant investigation.

Future developments in RA treatment will emphasize the practice of precision medicine, tailoring treatment plans based on patients' genetic makeup, immune system abnormalities, and disease progression.

The advancement of novel drug therapies will explore more targeted biologics and small molecule inhibitors to more effectively modulate immune system activity and slow disease progression. Moreover, the importance of early intervention and treatment strategies will be further recognized to minimize joint damage and functional impairment.

In terms of sustainability, personalized and targeted approaches to RA treatment will help reduce wastage of medical resources while enhancing patients' quality of life. Furthermore, continual progress in medical research will contribute to improving the efficiency and sustainability of healthcare facilities. However, it's important to note that the development of novel drugs and personalized treatments may bring new challenges, including issues of drug cost and accessibility, necessitating collaborative efforts from the medical community and governmental bodies for resolution.

From basic to clinic, psoriatic arthritis & axial spondyloarthritis

從基礎研究到臨床實證，乾癬性關節炎與中軸脊椎關節炎

Yi-Tsu Chuan

全以祖

Department of Rheumatology, Allergy & Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, ROC

林口長庚紀念醫院 風濕過敏免疫科

The interrelationship between psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA) has been a focus in the medical field from basic research to clinical evidence. Basic research indicates a close association between both diseases and immune system dysregulation, including excessive activation of immune cells such as T cells and dendritic cells, as well as overproduction of inflammatory mediators. Moreover, recent studies have found overlaps in immune modulation and inflammatory pathways, such as the IL-17 and IL-23 pathways, suggesting shared pathophysiological mechanisms and therapeutic targets between PsA and AxSpA. Specific genetic factors are also believed to play crucial roles in the development of both arthritides.

In clinical evidence, numerous studies emphasize the distinct phenotypes and clinical features of PsA and AxSpA, aiding in more accurate diagnosis and differentiation of the two diseases. Imaging modalities such as X-rays, MRI, and ultrasound play critical roles in diagnosing and monitoring disease activity. Therapeutically, significant progress has been made in managing these diseases with traditional disease-modifying antirheumatic drugs (DMARDs), biologics, and targeted therapy drugs.

In-depth research into PsA and AxSpA contributes to a better understanding of the pathophysiological processes of these diseases and provides a theoretical basis for the development of new therapeutic approaches. These studies not only offer clinicians more treatment options but also provide more effective strategies for patient treatment and management.

The comprehensive investigation into PsA and AxSpA aids in understanding the pathophysiology of these diseases and facilitates the development of novel therapeutic strategies. These advancements not only broaden the treatment choices available to clinicians but also enhance the effectiveness of patient treatment and management.

Patient oriented decision making, from lab numbers to patient reported outcomes

病患導向的治療策略 - 從檢驗數據蛻變到病人的主觀感受

Tsu-Yi Hsieh

謝祖怡

Department of Immunology and Rheumatology, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 免疫風濕科

Patient-oriented treatment strategies prioritize patients' subjective experiences and overall well-being over solely relying on objective data. This approach, including personalized treatment based on genetic, biomarker, and lifestyle factors, aims to optimize treatment outcomes.

Incorporating shared decision-making, medical teams collaborate with patients to consider their values and preferences in treatment decisions. Patient-reported outcomes, such as quality of life and pain levels, are crucial indicators of treatment effectiveness. Holistic care ensures comprehensive support for patients' physical, psychological, social, and spiritual needs.

Patient-centric strategies result in more effective and personalized treatments, enhancing overall patient satisfaction and outcomes. Shared decision-making fosters better communication and trust between patients and healthcare providers, thereby boosting treatment adherence.

Patient-oriented treatment strategies revolutionize medical care by prioritizing patients' well-being, incorporating shared decision-making, and providing holistic support. By empowering patients to actively participate in their treatment and considering their individual needs, these strategies ensure better treatment outcomes and overall quality of care.

The reflection of medical care from patient's perspective: Examples from SDM implementation in autoimmune disease and multidisciplinary care

從病人角度回饋於醫療照護：以 SDM 進行風濕疾病與整合醫療為例

Yen-Po Tsao

曹彥博

Division of Holistic and Multidisciplinary Medicine, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 全人整合醫學科

Shared decision making (SDM) provides an efficient and effective protocol for increasing healthy literacy of patients. SDM should be performed with best clinical evidence as well as expertise from physicians. SDM could become a bridge between clinical care and patients' expectations in determining the treatment choice, which could facilitate the decision-making process and to decrease the regret of medical choices. In this talk, we will provide SDM examples from autoimmune disease and multidisciplinary care through evidence-based implementation and patient-oriented practice. We hope to augment the satisfaction of clinical decision and compliance of medical treatment.

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多發性骨髓瘤標靶藥物及免疫治療的最新進展

The Landscape of Myeloma Targeted Therapy and Immunotherapy

時 間：113年6月22日 13:30-17:30

Time：June 22, 2024 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 6&7, Chih-Teh Building
Taipei Veterans General Hospital

多發性骨髓瘤標靶藥物及免疫治療的最新進展

The Landscape of Myeloma Targeted Therapy and Immunotherapy

Introduction of multiple myeloma

多發性骨髓瘤之臨床簡介

Hao-Yuan Wang

王浩元

Division of Hematology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 血液科 及 國立陽明交通大學 醫學系

Multiple myeloma (MM) is a hematologic malignancy characterized by the abnormal proliferation of plasma cells within the bone marrow. It represents the second most common hematologic cancer, accounting for approximately 1% of all cancers and 10% of hematologic malignancies. The disease typically arises in older adults, with a median age at diagnosis around 70 years, although it can occur in younger individuals.

The pathogenesis of MM involves the clonal expansion of malignant plasma cells, which produce excessive amounts of abnormal monoclonal immunoglobulins (M-proteins). These abnormal plasma cells accumulate in the bone marrow, leading to bone destruction, marrow failure, and the systemic manifestations of the disease. Common clinical features include bone pain, fractures, anemia, hypercalcemia, renal insufficiency, and increased susceptibility to infections.

Diagnosis of MM typically involves a combination of laboratory tests, imaging studies (such as X-rays, CT scans, or MRI), and bone marrow biopsy to confirm the presence of abnormal plasma cells. The disease is staged based on various factors, including the extent of bone disease, the level of monoclonal protein, and the presence of kidney dysfunction.

Treatment options for MM have expanded significantly in recent years, with advancements in chemotherapy, immunotherapy, targeted therapy, and stem cell transplantation. While MM remains largely incurable, these treatment modalities have improved outcomes and prolonged survival for many patients, particularly in the era of novel agents such as proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies. Ongoing research continues to explore new therapeutic approaches aimed at achieving deeper and more durable responses, with the ultimate goal of improving the quality of life and survival for individuals affected by this challenging disease.

Present treatment of multiple myeloma in Taiwan

現行台灣多發性骨髓瘤治療策略

Po-Shen Ko

柯博伸

Division of Hematology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 血液科 及 國立陽明交通大學 醫學系

In Taiwan, the treatment landscape for multiple myeloma (MM) mirrors global standards, with a multidisciplinary approach combining chemotherapy, immunotherapy, targeted therapy, and stem cell transplantation.

Chemotherapy remains a cornerstone of MM treatment in Taiwan, with regimens incorporating agents like bortezomib, lenalidomide, and dexamethasone being commonly used in both newly diagnosed and relapsed/refractory settings. These therapies aim to induce remission, control disease progression, and alleviate symptoms.

Immunotherapy has gained prominence in recent years, with the approval and adoption of monoclonal antibodies targeting CD38, such as daratumumab and isatuximab. These agents are used alone or in combination with chemotherapy, offering improved response rates and survival outcomes for MM patients.

In the realm of targeted therapy, proteasome inhibitors like bortezomib and carfilzomib play a crucial role in the treatment algorithm, inhibiting protein degradation pathways essential for MM cell survival. Additionally, immunomodulatory drugs (IMiDs) such as lenalidomide and pomalidomide exert direct antitumor effects and modulate the immune response against MM cells. For eligible patients, autologous stem cell transplantation (ASCT) remains a standard of care, offering the potential for deep and durable remissions. Maintenance therapy with lenalidomide post-ASCT has been shown to prolong progression-free survival in selected patients. Clinical trials evaluating novel agents, combination therapies, and personalized treatment approaches are ongoing in Taiwan, aiming to further optimize outcomes for MM patients. Collaborative efforts between clinicians, researchers, and healthcare institutions are instrumental in advancing the standard of care and improving the quality of life for individuals living with MM in Taiwan.

The landscape of myeloma targeted therapy and immunotherapy

多發性骨髓瘤標靶藥物及免疫治療的最新進展

Yao-Chung Liu

劉耀中

Division of Hematology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, National Yang Ming Chiao Tung University, Taipei,Taiwan,ROC

臺北榮民總醫院 內科部 血液科 及 國立陽明交通大學 醫學系

"The Landscape of Myeloma Targeted Therapy and Immunotherapy" refers to the current status and advancements in the treatment of multiple myeloma using targeted therapy and immunotherapy approaches. Multiple myeloma is a type of cancer that affects plasma cells in the bone marrow.

Targeted therapy involves using drugs or other substances to specifically identify and attack cancer cells while causing less harm to normal cells. Immunotherapy, on the other hand, works by harnessing the power of the immune system to recognize and destroy cancer cells

In the context of multiple myeloma, targeted therapy options include proteasome inhibitors, such as bortezomib and carfilzomib, immunomodulatory drugs, such as lenalidomide and pomalidomide, and monoclonal antibodies that target specific proteins on the surface of myeloma cells. Immunotherapy approaches in myeloma include immune checkpoint inhibitors, chimeric antigen receptor (CAR) T-cell therapy, and cancer vaccines.

Advancements in these targeted therapy and immunotherapy approaches have significantly improved outcomes for patients with multiple myeloma, leading to higher response rates, longer remission periods, and improved overall survival rates. Ongoing research and clinical trials continue to explore new treatment combinations and strategies to further enhance the effectiveness of these therapies.

Overall, the landscape of myeloma targeted therapy and immunotherapy is rapidly evolving, offering new hope and improved treatment options for patients with this challenging disease.

Clinical application of immunotherapy in multiple myeloma

免疫治療在多發性骨髓瘤的臨床運用

Chun-Kuang Tsai

蔡淳光

Division of Hematology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 血液科 及 國立陽明交通大學 醫學系

"Clinical Application of Immunotherapy in Multiple Myeloma" explores the evolving landscape of immunotherapy as a treatment modality for this hematologic malignancy. Immunotherapy capitalizes on the intricate interactions between the immune system and cancer cells to enhance antitumor responses.

Monoclonal antibody (mAb) therapy targets specific antigens on myeloma cells, triggering immune-mediated cytotoxicity or inhibiting crucial signaling pathways. Notably, agents like daratumumab and elotuzumab have demonstrated efficacy, either alone or in combination with conventional treatments.

Immune checkpoint inhibitors, primarily targeting PD-1/PD-L1 interactions, aim to counteract the immunosuppressive tumor microenvironment. Although initial trials showed modest outcomes, combination strategies exhibit promise in enhancing efficacy.

Chimeric antigen receptor (CAR) T-cell therapy represents a groundbreaking approach, genetically engineering patients' T cells to target B-cell maturation antigen (BCMA), a prevalent myeloma cell marker. Clinical trials have shown remarkable responses, albeit with associated toxicities.

Vaccine-based immunotherapy seeks to prime the immune system against myeloma-specific antigens, with early trials showing encouraging immunologic responses.

Overall, immunotherapy offers diversified strategies beyond conventional treatments in multiple myeloma management. While challenges like treatment resistance and toxicities persist, ongoing research holds promise for optimizing efficacy and safety, potentially improving patient outcomes.

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交叉前沿：探索微生物和免疫學對泌尿系統健康與治療的影響

Intersecting Frontiers: Exploring Microbial & immunological Influences in Urological Health & Therapeutics

時　間：113年6月22日　13:30-17:30

Time：June 22, 2024　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

交叉前沿：探索微生物和免疫學對泌尿系統健康與治療的影響
Intersecting Frontiers: Exploring Microbial & immunological Influences in Urological Health & Therapeutics

Exploring the association between gut and urine microbiota and prostate disease

探討尿液中微生物群與泌尿系統疾病之間的關聯

Hsiang-ying lee

李香瑩

Urology Department, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, ROC

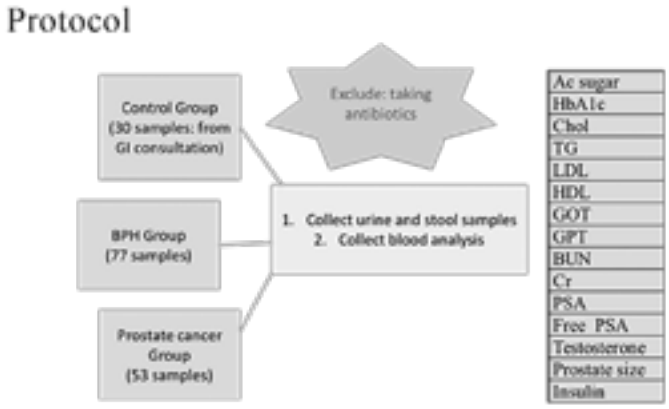
高雄醫學大學附設醫院 泌尿部

Background

Crosstalk between an organism and its gut commensal microbiota

Gastrointestinal microbiota

Indirect interactions such as regulation of the immune system, metabolism changes, and impacts on therapy(Influence on the cancer immune microenvironment, Influence in treatment response to agents, Chemotherapy and immunotherapy, Microbiota-driven tumorigenesis , From a state of microbial balance to a state of dysbiosis, Activation of Toll-like receptors, Genomic instability and DNA damage in host cells)



Results → Urine samples

(Stool samples are not significant difference)

Comparisons of demographic, clinical characteristics and bacteria alpha diversity

Correlation analysis:Positive correlation between bacteria and IPSS

Correlation analysis:Positive correlation between bacteria and IPSS subgroup

Conclusions

Significant difference of urine microbiota between control and stone diseases groups

Future: urine metabolites and microbiota

Stone culture to exclude infection stone ?

Distinctive features of gut microbiota in azoospermic men

無精症患者腸道與睪丸的微生物特徵

I-Shen Huang[a,b], Carl Jay Ballena Bregente[c], Tzu-Ping Lin[a], Cheng-Yen Kao[c], William J Huang[a,b]

黃奕燊 卡爾布雷根特 林子平 高正彥 黃志賢

[a] *Department of Urology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

[b] *Department of Physiology, School of Medicine, National Yang Ming Chiao Tung University. Taipei, Taiwan, ROC*

[c] *Institute of Microbiology and Immunology, College of Life Sciences, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC*

[a] *臺北榮民總醫院 泌尿部* [b] *國立陽明交通大學 生理研究所* [c] *國立陽明交通大學 微生物及免疫學研究所*

Background: Despite previous research revealing taxonomic disparities between the microbiomes of infertile men and healthy fertile controls, there remains limited understanding of the gastrointestinal microbiota's role in the development of male infertility. Our study focuses on elucidating the potential link between gut microbiota and defective spermatogenesis, particularly in the context of non-obstructive azoospermia (NOA) and obstructive azoospermia (OA). We aim to investigate correlations and identify pathogenic taxonomic units using stool samples obtained from individuals diagnosed with these conditions.

Methods: Stool samples were collected prospectively from 33 azoospermic men, consisting of 21 individuals diagnosed with NOA and 12 individuals diagnosed with obstructive azoospermia OA. The composition of the gut microbiome was assessed using a 16S rRNA gene-based sequencing protocol.

Results: Men diagnosed with NOA exhibited increased α diversity compared to OA counterparts. However, the composition of the microbiome (beta diversity) in NOA closely resembled that of the OA gut microbiome. Analysis at the phylum level revealed Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria as the dominant phyla, collectively accounting for 98.1% in the OA group and 98.2% in the NOA group. Predominant genera identified in OA included Phocaeicola, Mediteraneibacter, Escherichia-Shigella, Blautia, and Faecalibacillus, while those in NOA were Phocaeicola, Escherichia-Shigella, Mediteraneibacter, Bacteroides, and Bifidobacterium, respectively.

Conclusion: Our study investigated the gut microbiome composition in men diagnosed with OA and NOA, offering potential insights for novel treatments targeting defective spermatogenesis and aiding in its diagnosis.

Role of microbiome in kidney calcium oxalate stone formation

微生物相在含鈣腎臟結石形成的角色

Wei-Jen Chen

陳威任

Department Urology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 泌尿部

Calcium oxalate crystals, the predominant composition in kidney stones, arises from the oversaturation of calcium and oxalate ions in urine. Traditionally, high intake of oxalate-rich foods, imbalanced calcium consumption, impaired intestinal oxalate transport, and gastrointestinal malabsorption (e.g., post-gastric bypass surgery) were regarded as factors which can elevate oxalate absorption, consequently elevating urinary oxalate levels and the risk of kidney stone disease. The gastrointestinal microbiome, particularly enriched with oxalate-degrading bacteria, plays a crucial role in reducing oxalate absorption and urinary oxalate concentration by influencing the expression of oxalate transporters and net intestinal oxalate transport, leading to lower renal stone disease risk.

Traditionally, urinary tract was considered a sterile environment. However, using microbiota analysis methodology, studies suggest that urinary tract owns its unique microbiota, and is very different from gut microbiota. Recent studies also revealed the possible impact of the urinary microbiome in renal stone formation. In this mini-review, we reviewed recent evidence between the mechanism between urine microbiome and renal stone formation.

Urinary tract infections: Bacteria and host characteristics, antibiotic resistance, and recurrent infections

泌尿道感染：細菌與宿主特性、抗藥性與反覆性感染

Cheng-Yen Kao

高正彥

Institute of Microbiology and Immunology & Microbiota Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

國立陽明交通大學 微生物及免疫學研究所 & 微菌叢研究中心

The issue of antimicrobial resistance and recurrent urinary tract infections (UTIs) remains a critical concern in clinical practice. In our previous research, we conducted a comparative analysis of *Escherichia coli* strains isolated from urinary samples collected during two time periods, 2009-2010 and 2020, revealing variations in bacterial characteristics. Furthermore, we identified a direct association between the characteristics of *E. coli* strains and the attributes of the host. Specifically, our observations indicated that *E. coli* strains isolated from elderly individuals exhibited heightened resistance to antimicrobial agents and fewer virulence factors. Notably, a significant proportion (77.4%) of strains isolated from the 0 to 3 age group belonged to phylogenetic group B2. Antimicrobial susceptibility testing revealed a notable escalation in resistance among *E. coli* strains with advancing host age, with phylogenetic group B2 isolates displaying higher susceptibility to antimicrobial agents compared to isolates from phylogenetic groups A, B1, and D.

In our investigation aimed at assessing plasmid-mediated quinolone resistance (PMQR) in fluoroquinolone non-susceptible *E. coli* (FQNSEC) isolated from patients with UTIs, we observed a substantial prevalence of multi-drug resistant (MDR) and extensively drug-resistant (XDR) *E. coli* among FQNSEC isolates. Additionally, we found that plasmids carrying the *qnr* gene exhibited high transferability, resulting in resistance to other classes of antimicrobials in the transconjugants. Through genome characterization of XDR-*E. coli* strain EC1390, we identified two plasmids that contributed to antimicrobial resistance, bacterial growth in nutrition-limited environments, biofilm formation, and cell adhesion.

Furthermore, our findings indicated that uropathogens in recurrent UTIs exhibited greater virulence in genetically closely related *E. coli* strains. The heightened bacterial virulence observed in the younger age group (<20 years) and in patients without anatomical/functional defects or immune dysfunction suggests that virulent uropathogenic *E. coli* strains play a crucial role in the development of recurrent UTIs in otherwise healthy individuals. Additionally, prior antibiotic therapy, particularly fluoroquinolones administered within three months, could induce subsequent antimicrobial resistance in genetically closely related *E. coli* strains, thereby contributing to recurrent UTIs.

Investigation of bacterial interplay between strains and bacterial pathogenesis in polymicrobial urinary tract infections

以泌尿道感染之尿液培養研究多重菌株的交互作用與致病機轉

Chih-Chieh Lin

林志杰

Division of Urology, Department of Surgery, Taipei Veterans General Hospital, Taipei Taiwan, ROC

臺北榮民總醫院 泌尿部

Background and Objectives: Urinary tract infection is the most common bacterial infection globally, making it a significant public health concern. While cases caused by Escherichia coli are the most prevalent, other strains such as Staphylococcus belonging to Gram-positive cocci and Enterococcus species are also opportunistic pathogens in urinary tract infections. However, the current understanding of the mechanism behind polymicrobial urinary tract infections remains unclear.

Methods and Processes: In this study, we collected forty-four sets of samples to explore the relationship between patients, polymicrobial pathogens, and the disease. To assess bacterial pathogenicity, we employed a model using wax moth larvae to simulate in vivo infection experiments. This allowed us to evaluate the differences in virulence between single bacterial strains and various combinations of two strains. Additionally, we examined the growth patterns using liquid culture media outside the host, observing whether the two strains mutually promoted replication or inhibited each other's growth. Furthermore, we investigated the expression of virulence factors related to urinary tract infections, such as the ability to synthesize biofilms. For example, we stained biofilms adhering to the bottom of a 96-well plate with 1% crystal violet solution after washing with phosphate-buffered saline and fixing with methanol. The quantification of growth was then performed by reading the absorbance values after dissolution in 95% ethanol.

Research Findings: Among the forty-four collected sample sets, the combination of Escherichia coli with Enterococcus faecalis was the most prevalent (13.64%), followed by combinations of E. coli with Klebsiella pneumoniae (9.09%) and E. coli with Pseudomonas aeruginosa and E. coli with Streptococcus agalactiae (6.82%).

Through the in vivo infection model with live animals, we identified five sets (Patients #4, #11, #16, #18, #24) where the strains displayed higher toxicity when co-cultured than when cultured alone. Conversely, another set (Patient #3) showed the opposite phenomenon. Subsequent experiments on the phenotypes will focus on the strains from these six sets with significant differences in toxicity.

In Patient #4, when culturing pathogenic bacteria in tryptic soy broth (TSB), the quantity of Enterobacter hormaechei significantly decreased when co-cultured with Staphylococcus aureus. Growth conditions for S. aureus were found to be inferior when cultured in mixed healthy human urine compared to TSB.

Regarding biofilm synthesis, significant differences in biofilm formation were observed on the second and third days for strains from Patients #3 and #4 when cultured alone or together. Patients #11, #18, and #24 exhibited significant differences on the first day, while Patient #16 did not show any significant differences.

Host characteristics associated with recurrent urinary tract infection

反覆性泌尿道感染的宿主特徵

Yu-Hua Fan

范玉華

Department of Urology, Taipei Veterans General Hospital, and Department of Urology, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 泌尿部 及 國立陽明交通大學 醫學院 泌尿學科

Recurrent urinary tract infection (UTI) stands out as a prevalent issue in urological clinics. Recent studies have unveiled new insights into recurrent UTI, positioning it as a distinct entity separate from the initial infection. The pathogenesis of recurrent UTI appears to involve two primary mechanisms: bacterial factors and deficiencies in host defense.

Among bacterial factors, the survival of bacteria in the urinary bladder post-antibiotic treatment and the subsequent development of intracellular bacterial communities emerge as pivotal contributors. Host defense deficiency, marked by impaired pathogen recognition and compromised urothelial barrier function, assumes a crucial role in this recurrence.

Essential risk factors for recurrent UTI encompass immunodeficiency and anatomical abnormalities in the urogenital tract. In otherwise healthy women, voiding dysfunction and behavioral factors contribute to an increased risk of recurrent UTI. Notably, factors such as sexual intercourse and estrogen deficiency in postmenopausal women exhibit the strongest associations with recurrent UTI.

Clinical evidence suggests that serum macrophage colony-stimulating factor and urinary nerve growth factor hold promise as potential predictive biomarkers for recurrent UTI. Efficacy in preventing UTI has been demonstrated in clinical trials for the oral immunoactive agent OM-89. Additionally, the latest guidelines endorse vaccines as a recommended preventive measure for recurrent UTI.

New breakthrough with ADC and CPI in metastatic urothelial carcinoma

抗體藥物複合藥及免疫檢查點抑制劑在轉移性泌尿上皮癌之突破

Jiun-I Lai

賴峻毅

Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 腫瘤醫學部

Metastatic urothelial carcinoma is a deadly disease with poor prognosis. For decades, the standard of care first line treatment is chemotherapy, and the 5-year overall survival is less than 10%. Many efforts have been made to develop novel agents and treatment for this disease, but until recently, most regimens have not been superior to conventional chemotherapy.

In the past few years, there has been a wave of breakthrough in this disease setting. The ADCs include enfortumab vedotin, Sacituzumab govetecan have shown great efficacy in this setting. Checkpoint inhibitors have also proven effective in the second line setting. Although the combination of checkpoint inhibitors to chemotherapy in first line have previously been unsuccessful, in 2023 two phase III clinical trials that combined checkpoint inhibitors to chemotherapy and checkpoint inhibitors to ADC have shown great efficacy in the 1st line setting. This has marked a new era in the treatment algorithm in the field of metastatic urothelial carcinoma.

In my presentation, I will review the novel breakthroughs regarding checkpoint inhibitors and ADC in metastatic urothelial carcinoma. I will discuss treatment concepts and algorithms for treatment planning in this disease setting, and provide a through review of the current state of art medical systemic treatment for metastatic urothelial carcinoma.

Breakthrough of adjuvant therapy in renal cell carcinoma

腎細胞癌手術輔助治療的突破

Tzu-Hao Huang

黃子豪

Department of Urology, Taipei Veterans General Hospital, Taipei Taiwan, ROC

臺北榮民總醫院 泌尿部

Adjuvant therapy after surgical resection for high risk renal cell carcinoma had been proposed in recent decades, while no definitive benefit has been established. Various tyrosine kinase inhibitors (TKIs) have been evaluated in clinical trials and only S-TRAC trial demonstrated a tangible progression-free-survival benefit.

The emergence of immunotherapy has brought great success in treating advanced renal cell carcinoma, and has spurred numerous trials aimed at expanding the adjuvant treatment landscape. Based on KEYNOTE-564 trial, pembrolizumab stands as the only medication that shows the overall survival benefit, whereas other immunotherapy agents could not reach improvement in the adjuvant scenario. Notably, there is no universally accepted model for estimating the risk of recurrence after nephrectomy, resulting in highly heterogeneous patient inclusion across trials. Meanwhile, research endeavors targeting histopathological features or biomarkers to identify high risk population are also ongoing.

Additionally, caution is warranted in interpreting the results of adjuvant therapy, given its fundamental disparity from treatments for advanced or metastatic diseases. Quality of life is another critical factor to consider in the context of adjuvant treatment. Thus, despite the promising outcome of KEYNOTE-564, the importance of appropriate patient selection remains paramount. Currently, many trials are actively underway, fostering hope for further advancements in this field.

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肝臟移植受贈者全方位照護新紀元

A New Era of Comprehensive Care for Liver Transplant Recipients

時　間：113年6月22日　13:30-17:30

Time：June 22, 2024　13:30-17:30

地　點：臺北榮民總醫院 中正樓10樓 一般外科會議室

Place：10F, The Conference Room, Chung Cheng Building
Taipei Veterans General Hospital

肝臟移植受贈者全方位照護新紀元

A New Era of Comprehensive Care for Liver Transplant Recipients

Significance of sarcopenia and ERAS in HBP surgery: What is real mini-invasive surgery?

肌少症和術後加速康復 (ERAS) 在肝膽胰手術中的意義：什麼是真正的微創手術？

Toshimi Kaido

海道利实

General Surgery Department, St. Luke's International Hospital, Japan

聖路加国際病院 消化器 一般外科

Sarcopenia, characterized by a decline in skeletal muscle mass and muscle strength or physical activity, is now accepted worldwide as a new geriatric syndrome. Recent studies have identified significant associations between sarcopenia and poor outcomes of various diseases including liver diseases (1-3). This article reviews the significance of preoperative sarcopenia to liver surgery, particularly liver transplantation (LT).

How to stabilize the liver transplant peri-operative course : From the aspect of cirrhosis physiology

如何穩定進行肝臟移植手術全期過程：以肝硬化生理學的觀點論述

Cheng-Yen Chen

陳正彥

Department Transplantation Surgery, Taipei Veterans General Hospital,Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 移植外科

Enhanced Recovery After Surgery (ERAS) is a multimodal surgical care approach aimed at achieving early rehabilitation for major surgical patients. Since its proposal by Kehlet et al. in 1997, the concept of ERAS was initially intended for colorectal surgery, and later established in this field. Since then, the concept of ERAS has been validated and further developed, being applied to solid organ transplantation. Despite explorations dating back to as early as 1990 when Kehlet et al. experimented with early extubation before formally introducing the concept of accelerated recovery in liver transplantation, yielding encouraging results, emphasis has been placed on the importance of anesthesia management for these patients.

Over the years, independent studies have confirmed the importance and effectiveness of other classic ERAS parameters, including preoperative nutrition, early mobilization, early feeding, and optimal pain management for liver transplant recipients. Combining considerations of all these parameters in classic large-scale ERAS methods for liver transplant patients, studies have employed multimodal approaches to evaluate ERAS in liver transplantation, focusing on measurable clinical endpoints. Results have shown significant reductions in hospital stay and improved postoperative recovery. Accelerated rehabilitation therapy can be safely applied to selected liver transplant patients, and its value merits further development.

The hopeful prospect of widespread application of ERAS in selected liver transplant recipients in the future is promising.

Enhanced recovery for liver recipient : What we do for perioperative care

肝臟受贈者之加速康復：手術全期麻醉照護的二三事

Shen-Chih Wang
王審之
Department of Anesthesiology,Taipei Veterans General Hospital,Taipei, Taiwan, ROC
臺北榮民總醫院 麻醉部

Considering the dramatic hemodynamic changes during liver transplant, liver recipients are vulnerable to organ damage. The challenge to improve quality of perioperative care is how to integrate what we already know into practice. The principles we followed for liver transplant perioperative care are

1. Adequate hydration: We use stroke volume variation derived from arterial blood pressure waveform to guide our isotonic crystalloid hydration.
2. Avoid unnecessary anesthetic agents use: We use BIS index and surgical pleth index to guide our anesthetic agents use.
3. Avoid unnecessary blood product use: After years of experience in TEG-guided transfusion strategy, we now transfuse our patient only for uncontrollable bleeding.
4. Avoid postoperative opioid use: We use rectus sheath catheter for local anesthetic infiltration after liver transplant. Our result indicates this is an effective and uncomplicated way to decrease postoperative opioid use.

To further individualize perioperative care for every liver recipient, we investigate the information hidden beneath arterial blood pressure waveform. Currently we are able to show that richer variation of arterial waveform morphology correlates to better outcomes. Such correlation cannot be explained by blood pressure read outs. Our finding may provide a potential way toward delicate hemodynamic management to each liver recipient.

Postoperative Enhanced Recovery After Surgery (ERAS) nutritional support: Application and efficacy in living donor liver transplantation

術後加速恢復療程（ERAS）營養照護在活體肝臟移植的應用與成效

Po-Shan Wu

吳柏姍

Dietetics and Nutrition Department, Taipei Veterans General Hospital,Taipei, Taiwan, ROC

臺北榮民總醫院 營養部

Nutrition plays a crucial role in Enhanced Recovery After Surgery (ERAS) programs, as 9-44% of surgical patients suffer from varying degrees of malnutrition. Malnutrition increase the risk of postoperative infections, prolong wound healing, and extend length of hospital stay. Therefore, preoperative nutritional risk screening and assessment are essential elements. For those identified with malnutrition, preoperative nutrition support at least 7 days is recommended. Additionally, preoperative carbohydrate therapy is advised to improve insulin resistance.

Postoperatively, early oral intake within 24 hours is encouraged, along with prevention of nausea and vomiting. If oral intake is not feasible, enteral nutrition is preferred over parenteral nutrition. Case studies have shown that a well-designed ERAS nutritional care protocol can improve the nutritional status in malnourished patients undergoing living donor liver transplantation, increase preoperative weight, shorten intensive care unit stays, maintain postoperative weight, enhance postoperative muscle strength, and improve daily functioning.

Rehabilitation for liver transplantation

肝臟移植術前術後復健

Yung-Chuan Chang
張詠荃
Surgery Department, Taipei Veterans General Hospital,Taipei, Taiwan, ROC
臺北榮民總醫院 外科部

Liver transplant recipients may suffer from problems such as decreased cardiopulmonary endurance, insufficient muscle strength, limited mobility, bedridden, and dependence of daily life functions before and after the transplant operation.

The course will briefly introduce about assisting liver transplant recipients to safely transfer, progressively perform rehabilitation exercises, improve cardiopulmonary endurance, and appropriately select assistive devices to improve activity performance in pre-operative and postoperative stage. Additionally, improving the safety of home environment when discharged, and then rebuilding the independence of daily life functions to optimize the quality of life after transplantation.

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多重抗藥性細菌以及黴菌最新治療趨勢

Update of theTreatment of Multidrug Resistant Organism and Invasive Fungal Infection

時　間：113年6月22日　13:30-16:50

Time：June 22, 2024　13:30-16:50

地　點：臺北榮民總醫院　中正12樓會議室

Place：12F, The Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

多重抗藥性細菌以及黴菌最新治療趨勢

Update of theTreatment of Multidrug Resistant Organism and Invasive Fungal Infection

Update of treatment of third-generation cephalosporin-resistant Enterobacterales

三代頭孢黴素抗藥性腸內菌的治療新知

Yi-Tsung Lin

林邑璁

Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan ,ROC

臺北榮民總醫院 內科部 感染科

The incidence of extended-spectrum β-lactamases-producing Enterobacterales (ESBL-E) infections increased rapidly in Taiwan, in large part due to a greater number of community-acquired infections. Routine EBSL testing is not performed by most clinical microbiology laboratories and non-susceptibility to ceftriaxone is often used as a proxy for ESBL production, although strains with other mechanisms may be falsely presumed to be ESBL-producers. ESBL are most prevalent in *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Proteus mirabilis*. CTX-M enzymes, particularly CTX-M-15, are the most common ESBLs worldwide. ESBLs other than CTX-M with unique hydrolyzing abilities are variants of narrow-spectrum TEM and SHV β-lactamases with amino acid substitutions, but they have undergone less clinical investigation than CTX-M enzymes. AmpC β-lactamases are β-lactamase enzymes that are produced at basal levels by many Enterobacterales and increased AmpC enzyme production resulting from inducible *ampC* expression can increase MICs to certain antibiotics, most notably ceftriaxone, cefotaxime, and ceftazidime. *Enterobacter cloacae* complex, *Klebsiella aerogenes*, and *Citrobacter freundii* are the most common Enterobacterales at moderate to high risk for clinically significant AmpC production. Several guidelines or guidance have been issued in recent years for the treatment of multi-drug resistant microorganism. IDSA guidance addressed the treatment for ESBL-E and Enterobacterales with moderate to high risk for clinically significant AmpC production due to an inducible *ampC* gene. ESCMID guidance addressed the treatment for third-generation cephalosporin-resistant Enterobacterales (3GCephRE). In this presentation, I will review the updated information for the treatment for 3GCephRE.

Update of treatment of carbapenem-resistant Gram-negative bacilli

Carbapenem 抗藥性的革蘭氏陰性菌治療的新知

Chih-Han Juan

阮志翰

Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan ,ROC

臺北榮民總醫院 內科部 感染科

Carbapenems have long been considered the mainstay of treatment for serious infections caused by Gram-negative bacilli. However, the emergence and spread of carbapenem-resistant Gram-negative bacilli (CRGNB), often associated with the production of carbapenemases, have severely limited the utility of these antibiotics. As a result, alternative treatment options must be considered.

Treatment of CRGNB presents a significant challenge in healthcare due to limited treatment options and increasing resistance rates worldwide. In recent years, there have been significant updates in the management of CRGNB infections, focusing on the development of new treatment strategies. This speech will provide a comprehensive overview of the current approaches to the treatment of CRGNB, highlighting the latest advancements and challenges in the field. These include the use of novel beta-lactam/beta-lactamase inhibitor combinations, such as ceftazidime/avibactam, ceftolozane/tazobactam, imipenem-cilastatin-relebactam, and meropenem/vaborbactam, which have shown promise in clinical trials. Furthermore, the repurposing of existing antibiotics, such as colistin and minocycline, has also been explored as potential treatment options for CRGNB infections.

Overall, the management of CRGNB infections requires a multifaceted approach that includes the development of new antibiotics, and the exploration of alternative treatment strategies. This speech will explore these various aspects of CRGNB treatment, providing clinicians with the latest information to guide their management decisions.

Update of treatment in MRSA and VRE

金黃色葡萄球以及腸球菌的治療新知

Yu-Chung Chuang

莊祐中

Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan ,ROC

臺大醫院 內科部 感染科

The increasing prevalence of multidrug-resistant organisms (MDROs) presents a significant challenge in healthcare, a situation exacerbated by the slow development of new antimicrobials. Among these, the ESCAPE pathogens, including Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant Enterococci (VRE), are particularly concerning.

While vancomycin has traditionally been the standard treatment for MRSA, its efficacy and safety are now under scrutiny. The current consensus recommends targeting an AUC/MIC ratio of 400–600 mg*hour/L for the effective treatment of serious MRSA infections. Advancements in the field have introduced emerging antimicrobials such as ceftaroline and novel glycopeptide antibiotics, which have shown efficacy against these resistant gram-positive bacteria. Studies suggest daptomycin may be more effective than vancomycin in treating MRSA bacteremia. Research is also focused on enhancing the effectiveness of vancomycin and daptomycin, including their combination with beta-lactams, particularly ceftaroline, and fosfomycin.

Linezolid currently stands as the only antibiotic approved for VRE infections. However, daptomycin, though not officially approved for VRE, is frequently used off-label, with recent studies suggesting it may rival linezolid in effectiveness for VRE bacteremia. Higher doses of daptomycin, exceeding the standard 6 mg/kg, are being considered for these cases. The latest guidelines recommend a dosage range of 8-12 mg/kg for *Enterococcus faecium* bacteremia. There was a tendency towards higher doses, such as > 11 mg/kg, being linked to improved outcomes. Furthermore, achieving optimal pharmacodynamic targets, measured by the AUC/MIC ratio, is crucial. Additionally, the combination of beta-lactams and fosfomycin with daptomycin is showing a synergistic effect in the treatment of VRE bacteremia.

This presentation will delve into these developments, discussing their clinical implications and the evolving strategies for managing MRSA and VRE infections.

Update of treatment of invasive fungal infection

侵入性黴菌感染治療新知

Un-In Wu

胡婉妍

Department of Medicine, National Taiwan University Cancer Center, Taipei, Taiwan ,ROC

Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan ,ROC

Department of Medicine, National Taiwan University College of Medicine, Taipei, Taiwan ,ROC

國立臺灣大學醫學院附設醫院癌醫中心分院

Invasive fungal infections (IFIs) represent a significant clinical challenge, particularly in immunocompromised individuals, necessitating constant updates in treatment strategies. Recent guidelines, including those for invasive candidiasis, cryptococcosis, and rare molds, have provided crucial insights into optimal management approaches.

Despite existing antifungal agents, limitations such as poor pharmacokinetic traits, toxicity, drug-drug interactions, limited clinical efficacy, and emerging antifungal resistance persist. Consequently, there is an urgent need for new antifungal agents to address these challenges. These new agents belong to well-known drug families like azoles, polyenes, or beta-D-glucan synthase inhibitors, or to families with entirely novel mechanisms of action. Some drugs have demonstrated a head start in terms of potential clinical implementation, showcasing promising pharmacokinetic profiles and potent antifungal activity.

In addition to advancements in treatment, recent developments have focused on preventive strategies, particularly in high-risk populations such as patients undergoing allogeneic hematopoietic stem cell transplant (HSCT). Moreover, updated recommendations for primary prophylaxis of IFIs in hematological patients and those receiving novel targeted therapies such as chimeric antigen receptor T-cell (CAR-T) therapy in acute myeloid leukemia (AML) have emerged. These recommendations aim to optimize prophylactic strategies and mitigate the risk of opportunistic infections in vulnerable patient populations.

These advancements underscore the dynamic landscape of IFI management, emphasizing the critical role of ongoing research efforts in developing innovative therapies and preventive strategies. Continued collaboration and guideline development are essential to further refine approaches and improve outcomes in the challenging realm of invasive fungal infections.

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胰臟癌治療新境界

Breakthrough in the Treatment of Pancreatic Cancer

時　間：113年6月22日　　13:30-17:30
Time：June 22, 2024　　13:30-17:30

地　點：臺北榮民總醫院　中正18樓會議室
Place：18F, The Conference Room, Chih-Teh Building
Taipei Veterans General Hospital

胰臟癌治療新境界

Breakthrough in the Treatment of Pancreatic Cancer

Update precision medicine in pancreatic cancer

胰臟癌最新精準醫療

Hung-Yuan Yu

于洪元

Division of Gastroenterology and Hepatology, Department of Medicine and Therapeutic and Research Center of pancreatic Cancer, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 胃腸肝膽科 及 胰臟癌治療暨研究中心

Pancreatic cancer is one of the most lethal malignancies which will soon be the secondary leading cause of cancer death in United States in 2030. More than half patients were diagnosed with advanced or metastatic disease. Therefore, systemic treatment plays an important role in pancreatic cancer treatment. Unfortunately, the effect of traditional chemotherapy was disappointed. Even though the chemotherapy has a great step in recent years, the median overall survival in metastatic pancreatic cancer was still less than one year. There is still an unmet need for pancreatic cancer treatment.

Despite the rapid progress of precision medicine, there was little breakthrough in the treatment of pancreatic cancer. In fact, we have got much more information about the genetics and transcriptomics of pancreatic cancer, but there were no agents that target the common genetic alterations, including KRAS, TP53, CDKN2A and SMAS4. In previous study, potentially actionable alteration was identified in 12-25% patients. In Know Your Tumor registry trial, significantly longer overall survival was observed in patients who received a matched targeted therapy. Homologous recombination repair (HR) deficiency (HRD) is identified in a significant minority of patients with pancreatic cancer. Germline BRCA1/2 and germline PALB2 are considered core HR genes, which are identified in 5-6% of unselected pancreatic cancer cases. In patients with gBRCA1/2 mutations, superior response was documented with platinum-based therapy. In 2019, Olaparib, a PARPi, was approved for patients with gBRCA1/2-mutant advanced/metastatic pancreatic cancer, as maintenance therapy. Mismatch repair (MMR) deficiency (MMRd) is a well-known tumor-agnostic biomarker for pembrolizumab and could be a predictor for immune check-point inhibitor. Despite several clinical trials for potential target therapies failed, there are still several ongoing clinical trials. We hope that we could treat each patient with a personalized treatment strategy to optimizing the clinical outcomes and improve patients' quality of life in the future.

Carbon ion therapy in pancreatic cancer

胰臟癌的重粒子治療

I-Chun Lai
賴宜君
Department of Heavy Particles & Radiation therapy and Therapeutic and Research Center of Pancreatic Cancer, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 重粒子及放射腫瘤部 胰臟癌治療暨研究中心

Pancreatic cancer is the fourth most common cause of cancer-related morality worldwide, and the prognosis remains poor despite aggressive therapy.

Treatment with carbon ions provides several unique physical and radiobiologic properties. Carbon ions exhibit a characteristic energy distribution in depth, known as the “Bragg Peak,” where low levels of energy are deposited in tissues proximal to the target, and the majority of energy is released in the target. Distal tissues receive little energy, although, unlike protons, there is energy deposited distally due to nuclear fragmentation. Additionally, a steeper lateral dose penumbra is observed at greater depths than with heavy ions, such as carbon, than with photons or protons. Furthermore, carbon exhibit a higher linear energy transfer (LET) than photons and protons. This leads to a higher relative biological effectiveness (RBE), where damage caused by carbon ions is clustered in the DNA, overwhelming the cellular repair systems. With a higher LET than other methods of radiation and the characteristics of the Bragg Peak, CIRT provides a promising treatment choice for providing higher doses to targets while reducing irradiation to organs at risk (OARs).

Here, we will demonstrate our treatment results in pancreatic cancer using carbon ion therapy combing with chemotherapy.

Minimally-invasive robotic pancreaticoduodenectomy

達文西機器手臂輔助胰臟微創手術

Shin-E Wang, Yi-Ming Shyr, Shih-Chin Chen, Bor-Uei Shyr, Bor-Shiuan Shyr
王心儀 石宜銘 陳世欽 石柏威 石柏軒
Division of General Surgery, Department of Surgery and Therapeutic and Research Center of Pancreatic Cancer, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 外科部 一般外科 及 胰臟癌治療暨研究中心

Pancreaticoduodenectomy, so-called “Whipple operation”, one of the most challenging procedure, is a time-consuming, tedious and technique-demanding complex operation. Traditionally, this procedure used to be performed usually by open approach, which would result in a large and painful wound. With the introduction of laparoscopic and robotic surgery, minimally invasive surgery (MIS) has emerged as a worldwide trend to improve wound cosmesis and mitigate the wound pain. Although MIS for pancreaticoduodenectomy has also been attempted at some centers, the role of MIS, either robotic or laparoscopic approach has not been well established for the complex pancreaticoduodenectomy.

Giving that laparoscopic pancreaticoduodenectomy has been limited by its technical complexity and the high level of advanced laparoscopic skills required for pancreatic reconstruction, robotic surgical system is introduced to overcome several limitations related to the laparoscopic approach. Providing high-quality three-dimensional vision, an optical high magnification, articulation of robotic instruments, greater precision with suture targeting, and elimination of surgeon tremor, robotic surgical systems innovatively perform more delicate and complex procedures involving extensive dissection and suturing technique such as pancreaticoduodenectomy. Although associated with longer operative time, robotic pancreaticoduodenectomy (RPD) has been claimed to have the benefits of less delayed gastric emptying, less blood loss, shorter length of postoperative stay, and lower wound infection rate, as compared with the traditional open pancreaticoduodenectomy (OPD). Moreover, RPD seems to be not only technically feasible and also justfied without compromising the survival outcomes for pancreatic head and ampullary adenocarcinomas.

Therefore, RPD could be recommended not only to surgeons but also to patients in terms of surgical feasibility, surgical outcomes and patient satisfaction.

Case sharing in multimodality treatment for locally-advanced pancreatic head cancer

局部晚期胰臟癌多型性治療經驗分享

Bor-Shiuan Shyr

石柏軒

Division of General Surgery, Departments of Surgery and Therapeutic and Research Center of pancreatic Cancer, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 一般外科 及 胰臟癌治療暨研究中心

Background

Locally advanced pancreatic head cancer were considered as unresectable disease; however, with the adaptation of neoadjuvant treatment with advanced modern radiotherapy technique, more-and-more studies demonstrated promising outcomes of such patients after receiving conversion surgical treatment. We hereby present our humble experience of the first case of initially unresectable locally advanced pancreatic head cancer treated with conversion pancreaticoduodenectomy surgery after neoadjuvant chemotherapy and carbon-ion radiotherapy.

Presentation of case

A 74-year-old man was initially diagnosed with locally advanced pancreatic head-to-uncinate process ductal adenocarcinoma with tumor encasing SMV/main portal vein and obliteration of splenic artery, common hepatic artery, and SMA (cT4N0M0). After receiving 8 weeks of neoadjuvant chemotherapy Gemcitabine (1000mg/m2 on day 1, 8, and 15 in 4 weeks cycle) followed by 12 fractions of concurrent carbon-ion radiotherapy, a dramatic decline in serum tumor marker CA 19-9 from 219 U/mL to 50.4 U/mL was observed. He then underwent another 7 weeks of maintenance chemotherapy with SLOG regimen (oral S-1, leucovorin, oxaliplatin, and gemcitabine) followed by conversion pancreaticoduodenectomy surgery with successful R0 resection. Narrowing of portal vein with massive ascites and micro liver abscess were observed after surgery, which were successfully treated by percutaneous portal vein stenting and intravenous antibiotic therapy.

Conclusion

This is our first case experience of initially locally advanced unresectable pancreatic head cancer successfully treated with conversion surgery after neoadjuvant chemotherapy and carbon-ion radiotherapy.

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全方位乳房影像新發展：由診斷到治療

Comprehensive Breast Imaging Updates: From Diagnosis to Treatment

時　間：113年6月22日　　13:30-17:30
Time：June 22, 2024　　13:30-17:30

地　點：臺北榮民總醫院 第三門診9樓創新沙龍
Place：The Clinical Innovation Center,
Taipei Veterans General Hospital

全方位乳房影像新發展：由診斷到治療
Comprehensive Breast Imaging Updates: From Diagnosis to Treatment

Applications of contrast-enhanced mammography in clinical settings

對比顯影乳房攝影之臨床應用

Kwang-Jane Lin
林寬仁
Department of Radiology, Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan, ROC
醫療財團法人辜公亮基金會和信治癌中心醫院 放射診斷科

CEM combines digital mammogram with administration of intravenous contrast medium in identifing neovascularity associated with breast malignancy. It has higher sensitivity, specificity, positive and negative predictive value as compared with ultrasound plus tomosynthesis. Its clinical applications such as: (1) abnormalites seen at screening mammogram ie. Masses, asymmetry, architectural distortion, microcalcifications (2) symptomatic breast disease ie. localized breast pain, palpable mass, nipple discharge. (3) disease extent of breast cancer. (4) Response to neoadjuvant chemotherapy. (5) as an alternative to MRI.

We have 274 CEM examinations during the period between 2021/10-2023/10 (total 300 examinations excluding 26 examinations of Ca. pre-treatment evaluation and Ca. pre-C/T or post- C/T evaluation). The causes of examinations: asymmetry 107(35%), calcifications 82 (27%), distortion 27(9%), mass 12 (4%), abnormal sonographic findings 21 (7%) and other causes. 29 cancers detected among 274 examinations, cancer detection rate: 10.5% (19 DCIS, 7 IDC, 2 ILC and 1 tubular. Ca.). No LN metastasis found in these 29 cancers detected, rate of early breast cancer was 86.2% (25/29) (DCIS plus less than 1 cm invasive Ca. without LN metastasis). Among these 29 cancers detected, 34.4 % Ca. were not diagnosed by mammogram; 65.5% Ca. were not diagnosed by sonogram. 24.1% Ca. were diagnosed by CEM only. CEM showed better performance in detection of early breast cancer.

DBT really helps! Some interesting cases from VGHTPE

數位斷層乳房攝影之臨床助益：臺北榮總範例分享

Yi-Chen Lai

賴亦貞

Division of Ultrasound and Breast Imaging, Department of Radiology, Taipei Veterans General Hospital, and National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 放射線部 超音波暨乳房影像醫學科

Digital breast tomosynthesis (DBT) has been widely applied to both screening and diagnostic mammography. The fundamental of DBT is using off-axis acquisitions shift to separate the objects in different heights, and reconstructing the data to generate images enhancing the objects from a giving height by shifting the projections. Synthetic Mammography (SM) derives from DBT slices. The purpose of SM is to eliminate double exposures for full-field digital mammography (FFDM) and DBT. DBT plus SM reduces approximately 45% dose compared with DBT plus FFDM.

DBT has not only reduced the recall rate but also increased the invasive breast cancer detection rate. We present our clinical experience with case sharing from our hospital that how DBT enhance our daily diagnosis in asymmetries, masses, architectural distortions and calcifications.

DBT improves the conspicuity and margin visualization of masses. DBT demonstrates better the identification and location confirmation of asymmetries. DBT also depicts more FFDM or spot compression occult and subtle architectural distortions. We can recognize the benign calcifications, such as skin calcifications and vascular calcifications easily by viewing the DBT slices. DBT is non inferior to FFDM with suspicious calcifications detection in breast cancer screening. DBT shows better distribution of calcifications.

DBT is the next generation of FFDM. DBT helps us find more breast cancer and dismiss the normals. We should be more confident with using DBT in the future.

Breast tissue signature recognition using hyperspectral imaging techniques in IVIM MR imaging

在 IVIM MR 成像中使用高光譜成像技術進行乳房組織特徵識別

Si-Wa Chan

陳詩華

Department of Radiology, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 放射線部

In lecture, we will explore a pioneering approach to breast cancer detection, stepping beyond the traditional delayed contrast-enhanced breast MRI (DCE-MRI), which, despite its sensitivity, struggles with distinguishing between benign and malignant tumors and carries the risk of contrast media toxicity. We'll introduce an innovative technique utilizing apparent diffusion coefficient (ADC) and intra-voxel incoherent motion (IVIM) parameters, aiming to overcome these challenges.

Using a 3T MR system, our technique involves capturing axial IVIM images via echo planar imaging (EPI), covering both breasts. This method is enhanced with spectral pre-saturation inversion recovery and diffusion sensitization, applying weighting factors across a broad spectrum. This detailed analysis enables the differentiation of breast tissue types with remarkable clarity, based on quantitative parameters and signal intensity decay maps. Our approach reveals distinct patterns in the quantitative values of glands and fat, providing deeper insights into breast tissue composition.

We also delve into hyperspectral processing for analyzing diffusion-weighted imaging (DWI) at varying b values. By integrating advanced methods such as kernel constrained energy minimization (KCEM), iterative KCEM (IKCEM), and deep neural networks (DNN), we aim to significantly improve tumor detection precision. The effectiveness of these techniques is evaluated using 3D receiver operating characteristic (3D-ROC) analysis, highlighting their potential to revolutionize breast cancer diagnostics.

This lecture is designed to shed light on a safer, more accurate approach to breast cancer detection, encouraging a move away from reliance on contrast media and towards enhancing diagnostic specificity and sensitivity. Our discussion promises to be an insightful journey into the future of non-invasive cancer diagnostics, marking a critical advancement in patient care and treatment strategy.

Vacuum-assisted breast biopsy for BI-RADS 4 findings: Technical aspects and postbiopsy management

以真空輔助乳房切片施行於 BI-RADS 4 病灶：技術面與術後處置探討

Jane Wang

王甄

Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 放射線部

The presentation will be focused on vacuum-assisted breast biopsy (VAB) by stereotactic (or tomosynthesis)-guidance and MRI-guidance.

VAB features minimally invasive approach to target breast findings with diagnostic accuracy close to excisional biopsy. Stereotactic-guided VAB is indicated for suspicious appearing findings (BI-RADS 4 findings) depicted on mammograms, especially for mammographic-visible microcalcifications.

Tomosynthesis-guided VAB is the advanced design of stereotactic-guided VAB, can further applicable for abnormal findings only or more depicted on tomosynthesis such as architectural distortion. Pre-biopsy survey includes imaging preview for lesion location, breast thickness, lesion types and number, coagulation profiles. The suggested VAB workflow and trouble-shooting issues will be presented and discussed. The B3 lesions indicate those of uncertain malignant potential at histopathology. The VAB-yielded B3 lesions cover a wide-range of pathological diagnosis such as ADH, FEA, classical lobular neoplasm, papillary lesions, radial scar, phyllodes tumor. The postbiopsy management for the various B3 lesions, and the postbiopsy complications will be presented.

MRI-guided VAB is exclusively performed for the suspicious findings depicted on MRI, especially for MRI-only lesions. MRI-suspicious findings can be re-evaluated by second-look ultrasound. There are possibilities that the biopsy findings via second-look ultrasound are not correlated with the MRI findings, therefore, it is appropriate to leave a clip for ultrasound-biopsied finding followed by MRI correlation to revalidate. The different vendor design of MRI-guided VAB will be presented. The postbiopsy management for procedure-related complications and B3 lesions from stereotactic/tomosynthesis-guided VAB also applies to MRI-guided VAB.

In conclusion, VAB is a minimally invasive approach for BI-RADS 4 findings with high accuracy. However, the prebiopsy evaluation and postbiopsy management are mandatory to improve patient care and clinical outcomes.

Ultrasound-guided vacuum-assisted excision: Clinical applications for benign breast tumor(s) removal

超音波導引真空輔助微創手術作為良性乳房腫瘤切除的臨床應用

Wen-Chiung Lin

林文瓊

Women's health center, Chung Shan Hospital, Taipei, Taiwan, ROC

中山醫院 婦女保健中心

The first consultant-led one-stop diagnostic breast clinic in the world was available in the 1990s. Women can be investigated appropriately using mammography, ultrasonography and cytology with immediate reporting. A breast clinic with a combination of breast imaging study and interventional procedures, provides an efficient and comprehensive process for breast tumor diagnosis and treatment.

Core-needle biopsy (CNB) was a well-established, valuable technique that was still used in most cases, whereas vacuum-assisted biopsy (VAB) is a more recent technique. VAB has proven clinical value and can be used under sonographic, mammographic, and magnetic resonance imaging guidance. This method has been proven reliable and should replace surgical biopsies. As of 2010, studies began to report the possibility of excising lesions using this method, either as a secondary benefit or as an initial indication, referring to it as vacuum-assisted excision (VAE). Since then, VAE has been ever more widely used in clinical practice.

In recent years, as interventional radiologists, we set up a brand new imaging-led breast intervention clinic using conventional imaging diagnostic tools, and implemented VAB/VAE to provide more rapid and comprehensive treatment/diagnosis of breast tumors.

To date, VAE has had numerous applications: for removal of benign lesions when patients need; for excision of previously biopsied lesions with a histological diagnosis of high risk or uncertain malignant potential (B3 lesions); and for a repeat biopsy in cases in which there is discordance between the radiological and pathological findings.

It is crucial for interventional radiologists to understand the current scenario and the potential applications of VAE, because it can change the clinical management of some breast lesions by updating practices over the years.

Cryotherapy in the management of breast cancer: Sharing of personal experience

冷凍治療於乳癌之應用：個人經驗分享

Hung-Wen Lai
賴鴻文
Comprehensive breast tumor center, Department of Surgery, Changhua Christian Hospital, Changhua, Taiwan, ROC
彰化基督教醫院 全方位乳房腫瘤中心

Breast cancer is the most common cancer in women in Taiwan, and the leading cause of death in women. Early diagnosis and appropriate treatment of breast cancer is very important. Surgery, radiotherapy, chemotherapy, endocrine therapy and target therapy are important treatments for breast cancer. Nowadays, for early stage breast cancer, surgical treatment had evolved from modified radical mastectomy to breast conserving surgery. Sentinel lymph node biopsy also replaced axillary lymph node dissection. Recently, non-surgical ablation is emerging as an alternative local therapy option for patients with early-stage breast cancer and encompasses two main types of percutaneous therapeutic procedures: radiofrequency ablation and cryoablation. Both techniques involve obliteration of a spherical lesion and feasibility studies have shown that complete tumor ablation is achievable with good or excellent cosmetic results. Although few clinical studies have directly compared non-surgical ablation with conventional surgical resection, observational studies indicate that clinical outcomes are favorable with acceptable rates of local control and no detriment to long-term survival. Cryoablation is a minimally invasive technique currently employed in breast cancer care, that uses freeze and thaw cycles to treat benign breast lesions, small breast cancers or focal sites of metastatic disease in patients not eligible for surgery. The final goal of this procedure is to destroy breast cancer cells using extreme cold. In addition, several studies have shown that this technique seems to have an enhancing effect on the immune response, especially by increasing the expression of tumor neoantigens specific to tumor cells, which are then attacked and destroyed. Exploiting this effect, cryoablation in combination with immunotherapy could be the key to treating early-stage breast cancers or patients who are unsuitable for surgery. The preliminary experience of cryoablation used in the treatment of breast cancer and a literature review would be performed in the presentation.

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消化內視鏡於食道逆流及小腸疾病精準照護之新進展

Precision Care for GERD and Small Bowel Disease: Update in GI Endoscopy

時　間：113年6月22日　13:20-17:10

Time：June 22, 2024　13:20-17:10

地　點：臺北榮民總醫院　長青樓護理館會議室

Place：Nursing Arts Laboratory, Evergreen Building, Taipei Veterans General Hospital

消化內視鏡於食道逆流及小腸疾病精準照護之新進展

Precision Care for GERD and Small Bowel Disease: Update in GI Endoscopy

Current understanding of GERD in Taiwan

臺灣現今胃食道逆流疾病之認識

Ping-Huei Tseng
曾屏輝
Departments of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ROC
臺灣大學附設醫院 內科部

The prevalence of gastroesophageal reflux disease (GERD) has been increasing rapidly in Taiwan in recent decade, mostly related to the westernization of life style and diet. GERD is associated with a broad spectrum of symptoms, and have a great impact on the quality of life of patients. Currently, proton pump inhibitor (PPI) remains the most potent anti-secretory agent for acid suppression, symptomatic relief and mucosa healing, and is the drug of choice in the treatment of GERD. However, up to 40% of patients have poor responses to PPI. The underlying pathophysiology involved in refractory GERD is complex. Identifying factors that might attribute to the poor treatment response of PPI in GERD is very important to improve the overall treatment responses. Currently, endoscopy is the mainstay of diagnostic tool for patients with reflux symptoms in Taiwan, but a great proportion of patients have no esophageal mucosa changes on examination, so call non-erosive reflux disease (NERD). The 24-h MII-pH catheter combines impedance channels to conventional pH catheters and helps to establish the reflux-symptom association with symptoms index (SI) and symptom association probability (SAP), and therefore is very useful in clarifying the underlying mechanism of refractory GERD. With the aid of 24-h MII-pH monitoring, traditional GERD patients, who are quite heterogeneous from a pathophysiological point of view, could be further categorized into 1. endoscopic positive; 2. true NERD (patients with an excess of acid reflux); 3.hypersensitive esophagus to acid reflux; 4.hypersensitive esophagus to non-acid reflux) and 5.functional heartburn. For patients who could not tolerate catheter-based ambulatory MII-pH monitoring, utilization of prolonged wireless reflux monitoring off PPI therapy also helps to characterize severity of GERD. Absence of pathologic acid exposure on ambulatory reflux monitoring (AET <4.0% on all 4 days of the prolonged wireless pH study) with a normal endoscopy rules out GERD. Erosive esophagitis of Los Angeles Grade B or higher, and/or AET >=6.0% on 2 or more days constitutes conclusive GERD evidence. Therapeutic strategies should be directed based on the GERD phenotype and start with the least invasive and safest treatment options. Moreover, personal factors focused on visceral anxiety and hypervigilance need to be addressed because these features can affect symptom severity and health care use. These motility studies, including HRM, MII-pH, and wireless pH monitoring, are increasing adopted for clinical management of GERD in Taiwan, and could help to clarify the mechanism of refractory reflux symptoms and tailor treatment strategies (personalized/precision medicine).

Artificial intelligence in diagnosis of GERD

人工智慧運用於高解析度食道動力學檢查

Ming-Wun Wong

翁銘芠

Division of Gastroenterology, Department of Medicine, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan, ROC

佛教慈濟醫療財團法人花蓮慈濟醫院 內科部 肝膽胃腸科

The global and Asian prevalence of gastroesophageal reflux disease (GERD) is high and continues to increase. Esophagogastroduodenoscopy (EGD) is commonly utilized as the initial diagnostic test for individuals presenting alarm symptoms or those unresponsive to antisecretory therapy. However, the sensitivity of EGD in identifying reflux disease is not foolproof. When endoscopy fails to identify the cause of a patient's symptoms, ambulatory reflux monitoring is undertaken to confirm or dismiss a pathological esophageal reflux burden. Advances in metrics derived from pH-impedance monitoring are showing promise in enhancing GERD diagnosis.

Laryngopharyngeal reflux (LPR) symptoms, including voice hoarseness, sore throat, throat clearing, cough, and globus sensation, are attributed to the retrograde flow of gastric contents to the larynx, potentially causing laryngeal symptoms. However, determining whether laryngeal symptoms are directly caused by GERD remains a clinical challenge. Supragastric belching, characterized by the intake of air from the mouth/pharynx into the esophagus followed by immediate expulsion of esophageal air using abdominal straining, is often found in conjunction with GERD.

The incorporation of artificial intelligence (AI) in enhancing diagnostic accuracy for various diseases, including GERD, is gaining momentum. In this presentation, we will share our insights and provide an update on the current literature regarding the applications of AI in GERD diagnosis. This includes measuring novel pH-impedance metrics, evaluating LPR, and assessing supragastric belching. In conclusion, AI has shown high efficacy in measuring impedance metrics and is anticipated to play a significant role in optimizing the precise diagnosis and personalized management of GERD patients in the near future.

Personalized management of GERD

個人化胃食道逆流疾病之處置

Akinari Sawada
沢田明也
Department of Gastroenterology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan
大阪公立大學醫學研究所　胃腸部門

GERD is defined as a condition where the reflux of gastric contents causes troublesome symptoms and/or complications such as bleeding, stricture formation, and esophageal adenocarcinoma. GERD is one of the most common diseases in clinical practice as the prevalence of GERD is approximately 14% across the world. The pathophysiology of GERD is multifaceted, and reflux symptoms can be caused by several non-GERD conditions (i.e. disorders of gut-brain interactions including functional esophageal disorders and behavioral disorders). For the appropriate personalized management of GERD, it is essential to understand what accounts for the main pathophysiology of reflux symptoms in each patient using objective testing. On the basis of symptom profile, endoscopic findings and distinct patterns during ambulatory reflux monitoring, patients with reflux symptoms can be classified into four different phenotypes, erosive reflux disease (ERD), non-erosive reflux disease (NERD), reflux hypersensitivity (RH) and functional heartburn (FH). ERD and NERD are regarded as true GERD whereas RH and FH having normal esophageal acid exposure are classified as functional esophageal disorders. Surprisingly, RH and FH consist of up to 60% of endoscopy-negative reflux patients who are likely to benefit from pain modulators rather than acid suppressants. In addition, it has been increasingly recognized that an insignificant number of patients with behavioral disorders (i.e. excessive supragastric belching and rumination) could be misdiagnosed as GERD since they often manifest themselves as typical reflux symptoms such as heartburn and regurgitation. For these conditions, cognitive behavioral therapy should be considered instead of ineffective acid suppressants. As for true GERD, a new strong acid suppressant, P-CAB, has become available in several countries. However, there is still a paucity of evidence about the selection of treatment among PPI, P-CAB and anti-reflux surgery for true GERD.

Gel immersion endoscopy: An effective innovation for securing the visual field

凝膠浸入式內視鏡：一個用來保護視野的有效創新

Tomonori Yano

矢野智則

Department of Medicine, Division of Gastroenterology, Jichi Medical University, Tochigi, Japan

日本栃木市自治醫科大學 胃腸科

During endoscopy, especially in patients with gastrointestinal bleeding, it is often difficult to secure the visual field. Although water immersion techniques are sometimes used to mitigate this situation, maintenance of the visual field is often difficult because the injected water rapidly mixes with any luminal blood and/or residue. Poor preparation before colonoscopy also makes it difficult to secure the visual field when using water immersion or water exchange techniques. The use of gas insufflation to displace luminal contents can cause significant discomfort and difficult endoscope insertion.

We reported the technique called “gel immersion endoscopy”. Clear gel with an appropriate viscosity (which prevents rapid luminal mixing) is injected through the accessory channel, instead of water. The viscous gel displaces luminal blood, clots, and residue. In the space occupied by the gel, we can easily secure the visual field and perform endotherapy calmly and effectively, even in patients with massive arterial bleeding and/or poor preparation. Since the visual field can be secured even while the lumen is collapsed, the redundant scope loop is reduced, and maneuverability is improved. A low intraluminal pressure is maintained; this may reduce the patient’s discomfort and risk of complications.

We initially used a jelly-like drink “OS-1 jelly” (Otsuka Pharmaceutical Factory, Japan) for this technique. This is a dedicated rehydration-supplement for patients with dehydration composed of a gelling agent (polysaccharide-thickener), electrolytes, carbohydrates, and water. In this gel, mono-polar devices are less effective due to electrical current dissipation due to its high electrolyte content.

We developed the electrolyte-free gel dedicated to this method (Viscoclear, Otsuka pharmaceutical factory), launched in October 2020. It allows the effective use of mono-polar devices within the gel, and has been used in gel immersion EMR, gel immersion ESD. In addition, it has been used in various endoscopic procedures such as EUS, reduction of volvulus, and foreign body retrieval.

Novel advances in capsule endoscopy

膠囊內視鏡新進展

Yen-Po Wang

王彥博

Endoscopy center for Diagnosis and Treatment, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 內視鏡診斷與治療中心

Capsule endoscope was approved to be used for evaluation of small bowel disease since 2001. After 20 years, it had been regarded as the first option of examination for evaluation of suspected small bowel bleeding. Other than suspected small bowel bleeding evaluation, capsule endoscopy can also be used in Crohn's disease diagnosis and monitoring, celiac disease diagnosis, polyposis syndrome follow-up and evaluation of patients with suspected small bowel tumors. Capsule endoscopy was easy to be performed, less invasive, and less disruptive. Early capsule endoscopy can also help improve diagnostic yield in patients with suspected small bowel bleeding. In capsule endoscopy reading, the new generation of capsule endoscopy has longer battery life with real-time image detection that are useful in improving capsule endoscope completion rate. Double lens capsule endoscope and panoramic capsule endoscope were also developed to improve the diagnostic ability of capsule endoscopy. Panoramic capsule endoscope was found to increase the visibility of ampulla vater. Capsule retention happens in about 1% of examination. Risk factors evaluation, MR enterography/ CT enterography or patency capsule can help avoid capsule retention. Application of Artificial intelligence in assisting capsule endoscopy is developing in recent years. Artificial intelligence can help detect and classify different small bowel lesions, and also evaluation of visibility. In a recent prospectively conducted study, artificial intelligence-assisted reading was superior to standard reading in detecting P2 lesion and faster than standard reading. Artificial intelligence is promising to assist capsule endoscopy reading in the near future.

Novel advances in interventional enteroscopy

介入性小腸鏡新進展

Wen-Hung Hsu

許文鴻

Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Municipal Siaogang Hospital, Kaohsiung, Taiwan, ROC

高雄市立小港醫院 內科部 胃腸內科

Up to the end of the 20th century, the endoscopic options for diagnostic and therapeutic interventions throughout the entire small bowel were limited. In 2001, the introduction of double balloon enteroscopy by Pro Yamamoto opened the last “black box” of the gastrointestinal tract enabling complete visualization of the small bowel with non-surgical method. Currently, double-balloon enteroscopy, single-balloon enteroscopy, balloon guided enteroscopy and spiral enteroscopy are available in clinical practice. Recently, numerous new developments in the field of deep enteroscopy have emerged expanding the diagnostic and therapeutic application to against small bowel diseases with intervention such as tissue sampling with biopsies, mucosal injection, polypectomy, hemostatic techniques, stricture dilation, and retrieval of foreign bodies. Device assisted enteroscopy have become an important tool in the small bowel disease management.

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癌症婦女的生育能力保存

Fertility Preservation for Female Cancer Patients

時　間：113年6月22日　13:20-17:00

Time：June 22, 2024　13:20-17:00

地　點：臺北榮民總醫院　重粒子中心會議室

Place：Heavy Ion Therapy Center,
Taipei Veterans General Hospital

癌症婦女的生育能力保存
Fertility Preservation for Female Cancer Patients

Challenges in the treatment of ovarian aging: Exploring new strategies and approaches

面對卵巢老化的治療挑戰：新觀點與方法

Kuan-Hao Tsui

崔冠濠

Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC

高雄榮民總醫院 婦女醫學部

The aging process in the female ovaries involves a gradual decline in both the quantity and quality of oocytes. When this decline happens prematurely or accelerates, it leads to diminished ovarian reserve and/or ovarian dysfunction, significantly impacting a woman's reproductive and overall health, often resulting in infertility. The majority of clinically infertile patients are of advanced age, and ovarian aging is an irreversible phenomenon. Various factors such as mitochondrial DNA damage, telomere changes, reactive oxygen species, mitochondrial dysfunction, and known genetic mutations associated with primary ovarian insufficiency and reduced ovarian reserve play crucial roles in this process. In our comprehensive assessment of ovarian aging, we adopted a multi-omics strategy, leveraging various cutting-edge techniques. This included single-cell RNA-sequencing to delve into the transcriptomic profile of individual cells, spatial transcriptomics to study gene expression patterns in the context of tissue architecture, genomics to explore the entire set of genes in the genome, metabolomics to analyze the small molecules involved in cellular processes, and nutrigenomics to understand the interaction between nutrition and genes. To delve deeper into the mechanisms, we focused our investigations on target genes. This involved conducting *in vitro* studies in controlled laboratory environments, utilizing mouse ovaries as a model system, and analyzing germ cells obtained from aging patients. These diverse approaches allowed us to unravel the intricate details of gene expression, regulation, and function during ovarian aging. In clinical trials, we utilized nutrigenomics to identify small molecule drugs and nutritional supplements capable of enhancing energy metabolism and inducing microenvironmental changes in the germ cells of elderly infertile patients. By combining multi-omics with translational medicine, our research seeks to deepen the understanding of the molecular mechanisms underlying ovarian aging. This approach not only advances diagnostic capabilities but also paves the way for innovative treatment strategies.

Pregnancy in cancer survivors

癌症治療後的孕期照顧

Jian-Pei Huang

黃建霈

Department of Obstetrics and Gynecology, MacKay Memorial Hospital, Taipei, Taiwan, ROC

馬偕紀念醫院 婦產部

Nowadays, cancer survivors are gradually increasing as improvements in cancer diagnosis and treatment. It is important to recognize the impact of cancer and its treatment, such as operation, chemotherapy, or radiotherapy, on fertility and pregnancy outcomes. Although the fertility rate may be lower in cancer survivors, the pregnancy of them is not uncommon. The impact of previous cancer and its treatment on pregnancy, needs to be assessed and discussed with survivors by a multidiscipline team including oncologist, perinatologist, and associated specialists to support the complex cares for pregnant women after cancer assault.

The evidence of the association between miscarriage or spontaneous abortion and cancer treatment is mixed and varies with different patient cohorts and treatment modality. However, the congenital anomalies rate did not increase if avoid of chemotherapy or radiotherapy during 1st trimester. Although, most of the prenatal care in cancer survivors is the same as other pregnant women. However, there is still some concerns should be addressed. For example, in cervical cancer survivors who received conization, trachelectomy, or pelvic radiation, the incidence of preterm birth may increase. Therefore, the close follow up of preterm birth sign and cervical length may be warranted. Besides, the result of non-invasive prenatal test may be interfered by the cancer cells. Some reports that the incidence of gestational diabetes mellitus and pre-eclampsia going high of cancer survivors. However, the result is not consistent in literatures review. Other adverse pregnancy outcomes, e.g. high cesarean section and operative vaginal delivery rate, preterm birth, small for gestational age fetus, low birth weight newborn, NICU admission rate, and post-partum hemorrhage had been documented in some cancer survivors. The delivery method is major based on obstetric indication. But cesarean section is preferred in cervical cancer survivors after trachelectomy and pelvic irradiation which may cause abnormal birth canal. Breast feeding is not contraindicated in breast cancer survivors, especially feeding by the contralateral breast to avoid mastitis in irradiated breast and could be encouraged in most cancer survivors if they wish.

The effect of pregnancy on cancer outcomes depends on individual condition. Pregnancy could play a protective role or be a worsening factor, even though it doesn't have major effect in most cases. Therefore, either going for contraception or getting pregnancy should be a result of shared decision making by patients, families, and medical professionals.

Fertility preservation for gynecological cancer patients

婦科癌症患者的生育能力保存

Chi-Hong Ho

何積泓

Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 婦女醫學部

The incidence of gynecological cancers has been increasing in recent years. Due to advances in multimodality treatment, long-term survival is possible for many patients. For young patients who desire future pregnancy, it is necessary to preserve the reproductive organs and their function to prevent loss of fertility. However, for most cases of gynecological cancers, the standard treatment must have these organs removed. Close cooperation between oncologists, reproductive endocrinologists and obstetricians is necessary.

The fertility-sparing surgeries to treat cervical cancer include cervical conization, radical trachelectomy, and ovarian transposition before abdominal and pelvic radiotherapy. Radical trachelectomy is a curative procedure that allows for preservation of the uterine body, ovaries, and fallopian tubes. It is indicated for stage IA2/IB1 cervical cancer and for stage IA1 cervical cancer without vascular invasion.

For patients with endometrial cancer and precancer, fertility preservation should be considered for atypical endometrial hyperplasia and Grade 1 endometroid carcinoma that is localized to the endometrium. Hormone therapy with high-dose progestin is performed as fertility-sparing treatment. However, hormone therapy is not standard therapy for patients with endometrial cancer, and its eligibility must be determined comprehensively.

Fertility-sparing treatment of ovarian cancer can be considered in cases of stage I epithelial and sex cord-stromal ovarian cancer. The basic surgical approach recommended for fertility preservation consists of adnexectomy on the affected side, omentectomy, peritoneal cytology, peritoneal examination, along with pelvic and paraaortic lymph nodes dissection. In cases of germ cell tumor, fertility-sparing surgery is indicated for stage I–IV tumors. The BEP regimen (bleomycin, etoposide, and cisplatin) is very effective for germ cell tumors.

Laparoscopic ovarian transposition before and after chemoradiation in cervical cancer

子宮頸癌患者在化學放射療法前後之腹腔鏡卵巢轉位手術

Kuan-Gen Hung

黃寬仁

Department of Obstetrics and Gynecology, Linkou Chang Gung Memorial Hospital , Taoyuan, Taiwan, ROC

林口長庚紀念醫院 婦產部

Pelvic irradiation almost induces castration and long-term hormone therapy would then be indicated for young women. However, hormone therapy may raise problems of compliance and certain adverse side effects. For young women with invasive cancers need pelvic irradiation, preservation of ovarian function is crucial so that their qualities of life could be improved. Ovarian transposition has been proposed to preserve ovarian function in patients receiving radiation therapy for over forty years already.

Majority of ovarian transposition is requested by patients with fertility consideration or fear of long term exogenous estrogen replacement. Ovarian preservation seems mandatory for premenopausal young patient with non hormone-dependent gynecologic cancers or nongynecologic cancers requiring pelvic irradiation, based on the negligible chance of ovarian metastasis. This high anterolateral transposition of the ovary was not only distant away from the standard irradiated field for gynecologic cancer but also away from the extended radiation field.

We reported a laparoscopic technique for ovarian transposition in patients with invasive cancer before receiving pelvic radiotherapy. We use Lee-Huang point as the first entrance and as a landmark to transpose the ovaries to a high anterolateral position, 3-4 cm above umbilical line. It is a simple and effective procedure for the preservation of ovarian function and it does not complicate the subsequent therapeutic protocol. Although a long-term evaluation and a larger series are necessary, this procedure could be recommended to those premenopausal women who required pelvic irradiation, especially for those less than 40 years old.

Oocyte cryopreservation for cancer patients

癌症婦女的卵子冷凍保存

Shee-Uan Chen

陳思原

Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan, ROC

臺大醫院 婦產部

Advancements in cancer therapies have achieved much improvement in survival rate of cancer patients. The cancer treatments potentially damage their ovarian function. Therefore, the need for fertility preservation in cancer patients has increased. Appropriate controlled ovarian stimulation (COS) is important for fertility preservation with oocyte cryopreservation in female cancer patients. Most patients have only a single cycle opportunity owing to time constraints before oncologic treatment. Efficient and effective to obtain sufficient good quality oocytes with safety, including decrease of ovarian hyperstimulation syndrome (OHSS). Several protocols of GnRH agonist (long or short), GnRH antagonist, and progestin primed ovarian stimulation (PPOS) had been used. Which protocol is most suitable for cancer patients deserve investigation and discussion. What is the suitable dose for each patient. For the final maturation GnRH agonist trigger, hCG trigger or dual trigger based on follicle number, serum estradiol level, LH levels, and body weight are important.

Determination of the COS protocol and gonadotropin dose for oocyte cryopreservation in cancer patients requires an individualized assessment. To find the appropriate initial dosage of gonadotropin may be according to body weight, AMH, antral follicle count, BMI, and age. Adequate ovarian stimulation and duration (around 10 days) is important to obtain sufficient mature oocytes for fertility preservation. Recently, antagonist protocol or PPOS, feasible for GnRH agonist trigger if risk of OHSS, can decrease OHSS complication. These two protocols are also convenient and time-saving. Earlier counseling or random start can save the time for chemotherapy. Random-start ovarian stimulation for fertility preservation reduces time constraints without compromising oocyte yield and maturity. For estrogen-sensitive cancer, letrozole can be used during ovarian stimulation.

We started the oocyte cryopreservation program for unmarried female cancer patients of medical reasons since 2002. We have performed 115 cases in cancer patients. Breast cancer and hematological cancer were most common reasons. The mean age for freezing oocytes was 32 years. The mean number of oocytes frozen was 15. Ten cases underwent thawing. The usage rate was 8.8%. The mean storage duration was 5.0 years for those who thawed oocytes. The survival rate was 82% and fertilization rate was 76%. Two live births were obtained and one pregnancy got miscarriage. One patient was myelodysplastic syndrome after allogenic peripheral blood stem cell transplantation. The other patient was breast cancer after surgery and chemotherapy. The cumulative live birth per thawed case was 20%. The fertility preservation in cancer patients would be helpful for them to own biological children.

Cryopreservation of ovarian tissue

卵巢組織冷凍保存

Yu-Chiao Yi

易瑜嶠

Department of Obstetrics and Gynecology, Taichung Veterans General Hospital, Taichung, Taiwan, ROC

臺中榮民總醫院 婦女醫學部

Childhood and adolescent cancer survival has improved greatly these years. However, some of them will eventually have been sterilized by their chemotherapy. Though oocyte and embryo cryopreservation have been widely applied in female cancer victims for fertility preservation, they cannot be applied in adolescence. Ovarian tissue cryopreservation (OTC) is an important development for fertility preservation in girls and young women at risk of premature ovarian insufficiency as a result of treatment for cancer. Unlike traditional method like oocyte or embryo cryopreservation, ovarian tissue cryopreservation involves the removal and freezing of ovarian tissue containing primordial follicles, which can later be thawed and re-implanted or uses for in vitro maturation.

OTC offers several advantages, including the potential for preserving a larger number of primordial follicles compared to oocyte or embryo cryopreservation, making it particularly suitable for prepubertal girls and women with limited time for ovarian stimulation. Moreover, OTC allows for the preservation of hormonal function, which may contribute to better reproductive outcomes and overall quality of life post-treatment.

Despite its potential benefits, OTC presents challenges, including the risk of reintroducing malignant cells in cancer patients, the need for specialized expertise in ovarian tissue handling and cryopreservation techniques, and the uncertain long-term safety of re-implantation.

In conclusion, OTC represents a valuable option for fertility preservation in women facing gonadotoxic treatments. Continued research is needed to optimize the procedure, enhance follicle survival rates, and minimize the risk of reseeding cancer cells. Furthermore, efforts to improve access to OTC and address ethical considerations surrounding its use are essential to ensure equitable fertility preservation options for all women of reproductive age. Collaboration among oncologists, reproductive specialists, and patients is crucial to providing comprehensive care and support throughout the fertility preservation journey.

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免疫和細胞治療新進展學術會議

International Symposium on New Advances in Immune Cell Therapy

時　間：113年6月23日　09:00-12:30

Time：June 23, 2024　09:00-12:30

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

免疫和細胞治療新進展學術會議

International Symposium on New Advances in Immune Cell Therapy

Cell therapy: A new paradigm

細胞療法新典範

Shinn-Zong Lin
林欣榮
Neural Science Center, Hualien Tzu Chi Hospital Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan, ROC
佛教慈濟醫療財團法人 花蓮慈濟醫院 神經醫學科學中心

Exosomes, the extracellular vesicles secreted by various cells, have diverse biomolecules that modulate cellular functions in recipient cells.

Tumor-derived exosomes play the pivotal role in transferring oncogenic molecules to neighboring cells, leading to the alteration of their phenotype and promoting tumor growth, metastasis, drug resistance, and modulation of tumor microenvironments. Our research on malignant brain tumors has revealed that glioblastoma stem cells (GSCs) transfer their cargoes to tumor non-stem cells or normal cells via extracellular vesicles (EVs), leading to the development of a tumor stem cell subtype with therapeutic resistance and cancerous properties. TZAB-001, a monoclonal antibody produced from GSCs-derived extracellular vesicles, significantly reduce the therapeutic resistance of tumor stem cells by blocking the intercellular propagation of EVs. The TZAB-001 recognized proteins expressed in gliomas almost 60 times higher than other tumors. Immunohistochemical staining and western blot show that TZAB-001 antibody specifically recognizes human GBM stem cells, liver cancer cell line HepG2, pancreatic cancer cell PANC-1, and lung cancer cell line A549, but not normal brain cells. The results reveal that TZAB-001 has the application potential for tumor diagnosis, CarT immunotherapy in cancer stem cells, and ADC drug development to enhance their efficacy.

In regenerative medicine, exosomes derived from stem cells have shown promising results in promoting tissue repair and regeneration. Furthermore, exosomes also modulate the immune response and promote angiogenesis, which are critical processes for tissue regeneration. Our studies in Alzheimer's disease focus on developing a culture medium which can increase the exosomes production. Using mesenchymal stem cells (MSCs) and Trisomy-derived T21 AF-iPS cells co-culture system, we identify an exosome enhancer TZX4 that can significantly increase the production of exosomes. In addition, TZ-008 exosomes selected by small molecule BP, which significantly increase the production of the cytokine IL-34 to aid in treating Alzheimer's disease while reducing inflammatory cytokines such as IL-6 and IL-8. Furthermore, TZ-008 exosomes can directly reduce the production of amyloid beta proteins that lead to Alzheimer's disease.

The application of exosomes in regenerative medicine and cancer holds great promise. Nevertheless, there are still many challenges that need to be overcome. These include optimizing the isolation and characterization of exosomes, understanding their specific functions and mechanisms of action, and developing effective delivery strategies for clinical applications. Further research in these areas is needed to fully realize the potential of exosomes as a new class of therapeutics.

Targeted extracellular vesicles carrying nucleic acids for cancer therapy

攜帶核酸的靶向性細胞外囊泡用於癌症治療

L. James Lee

李 利

Institute of Biopharmaceutical Sciences, National Yang Ming Chiao Tung University, Taipei , Taiwan, ROC

Department of Chemical and Biomolecular Engineering, The Ohio State University, USA

國立陽明交通大學 藥學院 生物藥學研究所

美國俄亥俄州州立大學 化學及分子生物工程學系

Extracellular vesicles (EVs) are cell secreted particulates which contain rich biomolecules. EVs encapsulate genetic and proteomic materials have emerged as promising therapeutic agents because they are more biocompatible and can penetrate physiological barriers compared to synthetic nanoparticles. EVs are also much more affordable with lower immunogenicity than cell- or virus-based therapies. Here we show the development of a new bionanotechnology platform, cell nanoelectroporation (CNP), for highly effective cell transfection and production of EVs aplenty. The use of cell secreted EVs containing targeting ligands and therapeutic mRNAs and small RNAs is demonstrated in pre-clinical treatment of pancreatic cancer and brain caner. The potential of targeted EVs carrying therapeutic nucleic acids in immune therapies such as ADC (antibody-drug conjugate), ICI (immune check point inhibitor) and BiTE (bi-specific antibody T-cell engager) will also be discussed.

Stem cell therapy in knee osteoarthritis challenge and predicament

幹細胞在退化性膝關節炎的治療：挑戰與困境

Yu-Han Chang

張毓翰

Department of Orthopaedic Surgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan, ROC

林口長庚紀念醫院 骨科部 關節重建骨科

Stem cell therapy presents a promising avenue for treating knee osteoarthritis (OA), a widespread degenerative joint condition impacting millions globally. However, despite encouraging findings in preclinical studies and early clinical trials, numerous hurdles and uncertainties persist regarding its application in knee OA treatment.

Firstly, the absence of a standardized protocol for stem cell therapy in knee OA complicates result comparison across studies and clinics, casting doubt on treatment consistency and quality. Secondly, the efficacy and durability of stem cell therapy for knee OA remain under scrutiny, with varying outcomes reported. While some studies demonstrate significant pain relief and functional improvement, others yield only modest benefits or none at all. Furthermore, the duration of therapeutic effects remains uncertain, raising questions about the necessity for additional treatments over time.

Thirdly, the lack of FDA regulation in the United States leaves stem cell therapy for knee OA without standardized guidelines, resulting in divergent treatment approaches and potential safety risks. Lastly, the substantial cost associated with stem cell therapy poses a significant barrier to access, especially for patients without sufficient financial means or insurance coverage.

In essence, while stem cell therapy holds promise for knee OA treatment, numerous challenges persist. Further research is imperative to ascertain its safety and efficacy, alongside the development of standardized protocols and regulatory oversight. Additionally, efforts to improve access to stem cell therapy are crucial to ensure equitable treatment availability. In this presentation, I will also share my personal journey and experiences with utilizing allogeneic or autologous adipose-derived stem cell therapy for knee osteoarthritis (OA).

Semiconductor technology for cell therapy

半導體技術應用於細胞療法

Chen-Yi Lee

李鎮宜

Institute of Electronics, College of Electrical and Computer Engineering, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

國立陽明交通大學 電機學院 電子研究所

This talk will introduce the recent advances in semiconductor biochips realized by standard CMOS process. In the first part of this talk, several basic function modules such as location sensing, microfluidic operations, thermal control, tw-DEP sorting, and magnetic extraction will be introduced. Then bio-protocols for target medical tests can be derived from these basic functions to achieve better test accuracy and reliability. Two selected examples, LAMP COVID-19 test and stem cell quality detection, will be used to demonstrate the capability of the proposed semiconductor biochips. With more integrated functions in the proposed semiconductor chips and joint research in multidisciplinary collaboration, it is expected to see more successful stories in emerging medical applications in the very near future.

Current status and future challenges of cell therapy using induced pluripotent stem cells (iPSCs)

iPS 細胞細胞治療的現況與未來挑戰

Shinsuke Yoshida

吉田信介

Research and Development Center, CiRA Foundation, Kyoto, Japan

研究開發中心 公益財團法人京都大學 iPS 細胞研究財團

One of promising applications of human induced pluripotent stem cells (iPSCs) is cell therapy for many diseases. Many researchers have tried to generate cells or tissue-like structures, including organoids, which help to ameliorate target diseases. In Japan, the world's first autologous transplantation of iPS cell-derived cells (RPE cells) was carried out in 2014, and more than dozen clinical studies of allogeneic transplantation of iPS cell-derived cells have already been conducted, starting with also RPE cells since 2017. Until now (May, 2024) any severe adverse events related to transplanted cells have been reported.

To promote such allogeneic cell therapies, we, Center for iPS Research and Application (CiRA), Kyoto University, and CiRA Foundation spun out from there, have been contributed by establishing a clinical-grade haplobank of 27 iPSC lines from seven donors who were homozygous for one of the four most frequent human leukocyte antigen (HLA) haplotypes in Japan (Yoshida et al., 2023). This haplobank, which is in accordance with regulations and has been released since 2015, can provide HLA (HLA-A/HLA-B/HLA-DRB1) -matched iPSC lines to nearly 40% of the Japanese population. To overcome the HLA matching coverage limitations of this haplobank, we have also released other cell lines, including genome-edited hypoimmunogenic iPSCs covering a wider population.

We have another ongoing challenge, my iPS Project for low-cost autologous cell therapies through automation. Together with the findings on automation, we expect that many of the results of this project would be transferable to allogenic therapies as well. On the other hand, unlike the general-purpose haplobank for allogeneic transplantation, this project can focus more than ever on particular differentiated cells as well as iPSC, that would lead a better understanding of the quality of iPSC lines which is truly necessary for clinical applications. We expect that semiconductor technology can play an important role in achieving these two progress.

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牙髓疾病中的團隊作戰：
與牙周、贋復之跨科協同治療

Teamwork in Endodontic Disease: Interdisciplinary Treatment with Periodontics and Prosthodontics

時　間：113年6月23日　08:30-16:50
Time：June 23, 2024　08:30-16:50

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

牙髓疾病中的團隊作戰：與牙周、贋復之跨科協同治療

Teamwork in Endodontic Disease: Interdisciplinary Treatment with Periodontics and Prosthodontics

What you should know about periapical lesion

關於牙根病灶您應該了解的事

Yi-Ching Ho, Tienchun Kuo, Ian Chen, Yi-Chun Lin

何怡青 郭恬君 陳誼安 林怡君

Department of Stomatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Department of Dentistry, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Elite Dental Clinic, Taipei, Taiwan, ROC

臺北榮民總醫院 口腔醫學部

國立陽明交通大學 牙醫學系

協力牙醫診所

Typical periapical lesion is located at the root apex. When a lateral lesion appears around the root, in addition to vertical root fracture, the possibility of lateral canals, cementum tear, or root perforation must be considered. The prevalence of lateral canals is 27-75%. However, not all lateral root canals would cause lateral lesions. Only larger lateral root canals that are communicated with the periodontal tissue will increase the chance of lateral lesions. The instrumentation of root canal treatment cannot clean the lateral root canals. If the lateral lesions remain unhealed after root canal treatment, periapical surgery or intentional replantation will be indicated. Cementum tear is a special kind of root surface fracture, leading to periodontal and periapical destruction. The key treatment of cementum tear is to remove the fractured cementum. This requires interdisciplinary collaborative treatment between periodontist and endodontist. Besides, if root perforation occurs and is not repaired, lateral lesions and even periodontal pockets may appear. When treating root perforation, the time and location must be considered and the appropriate filling material must be determined.

When a large lesion appears, we should understand the success rate of non-surgical root canal treatment. When non-surgical root canal treatment fails, periapical surgery will be indicated. We will discuss the criteria to evaluate periapical healing after periapical surgery by radiographs or CBCT. When periapical surgery is combined with guided tissue regeneration, the periodontist will share with us how to choose bone graft materials and membrane for a successful surgery. Finally, we will share cases of soft tissue fenestration. The possible causes will be discussed, and cases of successful surgical treatment through interdisciplinary cooperation between periodontist and endodontist will be presented.

What you should know about cracked tooth

關於裂齒您應該了解的事

Chen-Yang Cheng, Yen-Chun Liu, Chia-Lun Tsai, Chun-Chi Peng
鄭陳陽 劉妍君 蔡佳倫 彭炯熾
Elite Dental Clinic, Taipei, Taiwan, ROC
Department of Stomatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
P & H Dental Clinic, Taipei, Taiwan, ROC
協力牙科
臺北榮民總醫院口腔醫學部
敦南牙醫聯合診所

The definition of a cracked tooth is that a thin surface disruption of enamel and dentin, and possibly cementum, of unknown depth or extension. Histological studies found that dentinal tubules were invaded by bacteria, especially when the crack extended perpendicularly into the dentin. In many cases, the crack extended to the pulp, leading to reactions with intensities ranging from acute inflammation to total pulpal necrosis. Due to incomplete fracture of the crown, various symptoms of pulpitis are caused, such as biting pain, rebound pain, sensitivity to cold and heat, sensitivity to sweets. Most patients with cracked teeth are middle-aged or elderly. Based on the enamel wear pattern, it is estimated that the longevity of teeth without modern care is about 30 to 40 years. Cracked teeth also often occur in patients who like to eat hard and crispy foods. There are strong masticatory muscles or attrition on occlusal surface.

The treatment for cracked teeth is to protect the affected teeth. We know that the earlier cracks are diagnosed, the greater the tooth's survival rate. However, no one has the "crystal ball" to foresee the future, but we now have outcome information to help guide us clinically. Informing the patient that the tooth is compromised or has a guarded prognosis is essential. The patient's understanding of treatment limits, bite force and eating habits are definitely important predictors.

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皮膚屏障的全面防護

Global Protection of Skin Integrity

時　間：113年6月23日　08:00-12:10

Time：June 23, 2024　08:00-12:10

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

皮膚屏障的全面防護
Global Protection of Skin Integrity

Bridging the science for patients with hidradenitis suppurativa: Inflammation on, below and beyond the skin

從皮膚內與外之發炎建構化膿性汗腺炎患者的科學研究

Chia-Bao Chu

朱家葆

Department of Dermatology, National Cheng Kung University Hospital, Tainan, Taiwan, ROC

國立成功大學醫學院附設醫院 皮膚科

Hidradenitis suppurativa (HS) is an underestimated serious skin disease, with debilitating consequences for the personal and professional lives of patients. The estimated prevalence of 1% is likely to be an undervaluation, since it is still often not recognized by physicians, despite increasing awareness for HS. In addition, there is a patient's delay in HS, as the patients hesitate to visit a physician, due to embarrassment for the disease, which can include lesions with foul smelling drainage. This often leads to a diagnostic delay of approximately seven years, in which the disease may progress. The exact pathophysiology of HS is not clarified yet and the clinical presentation is heterogeneous, which makes the treatment of HS challenging and the burden for patients tremendous.

Medical and surgical interventions are the two main therapeutic approaches for HS. Even though the latter is less well investigated, it remains one of the most effective treatment options for HS. However, surgery itself can add to the burden of patients, as the experience can be traumatizing, leaving the patients with conspicuous scars. Moreover, the clinical appearance of HS often does not correspond with the patient's own experience of her or his disease.

The chronic and unpredictable nature of HS can lead to fear, shame and inhibition of daily activities. Further increasing awareness and a better insight into the prevalence can help reduce the diagnostic delay and help initiate treatment earlier, decreasing the burden for the patient.

The aim of this lecture is to address different phenotype of hidradenitis suppurativa on, below and beyond the skin, and to describe how the cytokine elevated in hidradenitis suppurativa may affect the treatment decision and treatment expectation.

Now and future: Melanoma real world cases sharing under current reimbursement

健保制度下的黑色素癌實際案例分享：現在與未來

Yi-Shuan Sheen

沈宜萱

Department of Dermatology, National Taiwan University Hospital, Taipei, Taiwan, ROC

國立臺灣大學醫學院附設醫院 皮膚科

This session examines the efficacy and management of side effects in targeted therapy for melanoma. Targeted treatments, particularly BRAF and MEK inhibitors, have demonstrated notable success in impeding specific molecular pathways implicated in melanoma progression. Despite their efficacy, these therapies can induce diverse side effects, spanning from cutaneous reactions to systemic complications. Effective management of these adverse events is paramount for treatment adherence and patient well-being.

Strategies such as dosage adjustments, combination therapies, and supportive care interventions are pivotal in mitigating side effects while preserving therapeutic efficacy. Ongoing research aims to develop novel targeted agents with improved safety profiles. By integrating comprehensive side effect management strategies into treatment protocols, clinicians can optimize the therapeutic benefits of targeted therapy and improve outcomes for melanoma patients.

New treatment option for psoriasis: Otezla

乾癬治療新選項：Otezla

Shang-Hung Lin
林尚宏
Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ROC
高雄長庚紀念醫院 皮膚科

There are more and more treatment options for patients with psoriasis (PsO) to control disease activity and improve quality of life. The traditional topical drugs, phototherapy, and oral systemic drugs could be used to treat patients with moderate to severe PsO before biologic agents. Recently, there is a new option as apremilast, which brand name is Otezla, to be available and reimbursed in Taiwan since Mar. 1st this year. Although the efficacy of Otezla is similar with methotrexate, cyclosporine or acitretin, its unique safety spectrum can help patients to reduce concern on hepatotoxicity, nephrotoxicity, adverse events on cardiovascular system, lung or other organs.

As Otezla has been one of four systemic oral drugs to treat patients with moderate to severe PsO, let's review its profile and discuss how it can be utilized to benefit our patients clinically.

Optimized generalized pustular psoriasis patient journey and lead them to the future

引領健康未來：最佳化膿疱型乾癬的病患旅程

Chun-Bing Chen
陳俊賓
Department of Dermatology, Chang Gung Memorial Hospital, Taipei, Taiwan, ROC
林口長庚紀念醫院 皮膚科

The understanding, treatment, and overall management of generalized pustular psoriasis (GPP) remain unique challenges. Recent studies emphasize the necessity for optimized treatment patterns and improved treatment goal strategies, as detailed in a comprehensive patient long journey for the GPP management. There is the importance of personalized treatment plans tailored to meet the specific needs of GPP patients. Furthermore, addressing the unmet needs within the GPP community involves enhancing clinical understanding and care approaches. Innovative educational initiatives, aim to leverage data to transform patient care by educating healthcare providers on the latest research and treatment strategies. The future of GPP patient care relies heavily on continuous research, patient-centered care models, and the integration of new therapies that promise more effective management of the disease. Through collective efforts, the journey towards optimized patient care looks promising, with the ultimate goal of significantly improving the quality of life for individuals affected by GPP.

Field therapy of actinic keratosis

日光角化症的區域導向治療

Yen-Jen Wang
王研人
Department of dermatology, MacKay Memorial Hospital, Taipei, Taiwan, ROC
馬偕紀念醫院 皮膚科

Actinic keratosis is the most frequent premalignant skin disease in the white population with a prevalence of 37.5% among ≥ 50 years of age. In Taiwan, the prevalence was 0.056%-0.066% over 45 years old but may be under-estimated. If left untreated, actinic keratosis may develop into squamous cell carcinoma (SCC). Percentages reported in studies range from 0.025 to 16% per actinic keratosis lesion per year.

Field-directed therapies are preferred for not only therapeutically effective but have a prophylactic effect on preventing new lesions and development of SCC. Currently the treatment choices included 5% fluorouracil cream, 5% imiquimod cream, and photodynamic therapy (PDT).

The newly available medicament Tirbanibulin Ointment 1% has received FDA and TFDA approval in the treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis of the face or scalp in adults. The mode of action included microtubule inhibition and cell death by apoptosis. From 2 phase 3 trials, ≧ 75% clearance rate was achieved 8 weeks after treatment starts. Adverse events are majorly local skin reactions including flaking and erythema.

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邁向甲狀腺癌的個人化醫療

Towards Personalized Medicine in Treatment of Thyroid Cancers

時　間：113年6月23日　08:20-12:00

Time：June 23, 2024　08:20-12:00

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

邁向甲狀腺癌的個人化醫療

Towards Personalized Medicine in Treatment of Thyroid Cancers

Preoperative molecular testing for thyroid cancers

甲狀腺癌術前分子診斷

Chin-Sung Kuo

郭錦松

Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 內分泌暨新陳代謝科

Thyroid cancer commonly presents oncogenic genetic alterations, The *BRAF* V600E mutation is the most frequently observed, primarily in papillary thyroid carcinoma (PTC). Molecular genetic testing performed before thyroid nodule surgery has demonstrated effectiveness in improving diagnostic accuracy, thereby contributing to the reduction of unnecessary thyroidectomies.

We introduce a case involving the Bethesda system (TBS) category III thyroid nodule harboring a positive *BRAF* V600E mutation detected via qPCR assay, followed by thyroidectomy and lymph node dissection. Nevertheless, the definitive pathology report yielded an unexpected diagnosis of indolent follicular thyroid carcinoma accompanied by a rare non-V600E *BRAF* mutation, V600_K601insNTV, mutation confirmed by Sanger sequencing. The case presented highlights the critical need to thoroughly evaluate molecular genetic testing results in thyroid nodule FNA cytology, particularly in cases with borderline Ct values detected by qPCR assays.

Furthermore, we share the experience of a TBS VI thyroid nodule with molecular testing. The 31-year-old woman without underlying diseases discovered a thyroid nodule as a solid, hypoechoic, wider-than-tall nodule measuring 11.8 × 10.2 × 12.4 mm in size. Fine-needle aspiration cytology was classified as TBS VI, and the diagnosis was PTC. To screen for common genetic alterations, the analysis did not reveal the presence of mutations such as *BRAF V600E*, *NRAS Q61R*, *NRAS Q61K*, *HRAS Q61R*, or *HRAS Q61K* mutations nor fusions of *CCDC6-RET*, *NCOA4-RET*, *PAX8-PPARG*, *ETV6-NTRK3*, *TPM3-NTRK1*, *IRF2BP2-NTRK1*, or *SQSTM1-NTRK1*. Subsequently, the patient underwent total thyroidectomy and central lymph node dissection to make a pathological diagnosis of cribriform and morular cribriform morular thyroid carcinoma.

Molecular testing performed before thyroid nodule surgery has demonstrated effectiveness in improving diagnostic accuracy.

Preoperative diagnostic ultrasound for thyroid cancers: Focus on TIRADS

甲狀腺癌的術前超音波診斷

Chun-Jui Huang

黃君睿

Division of endocrinology and metabolism, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 內分泌暨新陳代謝科

Ultrasound risk stratification systems for evaluation of thyroid nodules are important to estimate the risk of malignancy and determine whether fine needle aspiration (FNA) should be performed. Diagnostic ultrasound is the first step to diagnosis of thyroid cancer.

The American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) Committee has proposed a point score system using the sum of points for individual sonographic features to assess incidental thyroid nodule. A sum of point ≥7 is indicative for FNA in nodules ≥ 1 cm, whereas a sum of point 3 or 4-6 is indicate for FNA in nodules ≥ 2.5 or ≥ 1.5 cm. The American Thyroid Association (ATA) has also published guidelines for thyroid nodules describing a pattern based atlas without points. The ACR-TIRADS and ATA share commonalities regarding sonographic features for high risk (hypoechogenicity, punctate echogenic foci, irregular margins, taller than wide shape) and very low risk (entirely cystic nodules or spongiform appearance) nodules. For low to intermediate suspicious nodules, the two systems differ in size cutoffs for FNA. The ATA system is more sensitive but less specific due to lower FNA size cutoffs.

The strength of ACR-TIRADS lies in the harmonization of the reporting of nodules and classification of all possible sonographic appearances. In contrast, 7.8% of the nodules are not classifiable by the current ATA system. The ATA is drafting an updated guideline to include new evidences for the literature including the findings of macrocalcification as an independent predictor for high malignancy risk in solid nodules and the significance of marked hypoechogenicity compared to not marked hypoechogenic nodules. A review of sonographic pattern of thyroid nodules shall be presented in this section.

Transoral endoscopic thyroidectomy: A paradigm shift in thyroid surgery

經口甲狀腺切除術

Jui-Yu Chen

陳瑞裕

Division of General Surgery & Thyroid Medical Center, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 外科部 一般外科暨甲狀腺醫學中心

Transoral endoscopic thyroidectomy, especially the vestibular approach, is a groundbreaking surgical technique that has revolutionized the field of thyroid surgery. Pioneered by Dr. Angkoon Anuwong, this innovative approach represents a significant departure from traditional open thyroidectomy methods. By utilizing endoscopic instruments inserted through small incisions in the oral cavity, transoral endoscopic thyroidectomy offers patients the benefits of scarless surgery and improved cosmetic outcomes.

Indications for transoral endoscopic thyroidectomy encompass a wide range of thyroid pathologies, including benign thyroid nodules, Graves' disease, and select cases of thyroid cancer. It's crucial to note that the procedure's suitability for thyroid cancer is limited to tumors of relatively small sizes, tumor locations and the surgeon's confidence in performing the procedure safely and effectively. Patient selection criteria are carefully evaluated to ensure optimal outcomes, with emphasis placed on appropriate anatomical considerations and pathological characteristics. With advancements in surgical techniques and instrumentation, transoral endoscopic thyroidectomy has become increasingly versatile and applicable to a broader range of thyroid conditions.

The future trend of transoral endoscopic thyroidectomy is characterized by ongoing advancements aimed at further enhancing its safety, efficacy, and applicability. Continued research and development efforts focus on refining surgical techniques, optimizing patient selection criteria, and integrating innovative technologies such as robotic-assisted surgery. Additionally, the evolution of transoral endoscopic thyroidectomy is expected to lead to improved patient outcomes and shorter recovery times, further solidifying its role as a cornerstone of modern thyroid surgery. These advancements also target the reduction of procedure-related complications, such as mitigating the risk of injury to adjacent structures like the mental nerve, alleviating postoperative discomfort, and lowering the incidence of surgical site infections. These strides in enhancing safety and efficacy contribute to heightened patient confidence and satisfaction, positioning transoral endoscopic thyroidectomy as an increasingly preferred choice for thyroid surgery.

In conclusion, transoral endoscopic thyroidectomy represents a paradigm shift in the field of thyroid surgery, offering patients a scarless and cosmetically favorable alternative to traditional open procedures. With its origins rooted in the pioneering work of Dr. Angkoon Anuwong and ongoing advancements in surgical techniques and technology, transoral endoscopic thyroidectomy is redefining the landscape of thyroid surgery and holds great promise for the future of patient care.

Target therapy in advanced thyroid cancers

晚期甲狀腺癌的標靶治療

He-Jiun Jiang

姜和均

Division of Endocrinology and Metabolism, Department of Internal Medicine, E-Da Dachang Hospital, Kaohsiung, Taiwan, ROC

義大大昌醫院 內分泌新陳代謝內科

Thyroid cancer is the most prevalent endocrine malignancy, with differentiated thyroid cancer (DTC) making up the majority of cases. Standard treatments for DTC typically include surgery, radioactive iodine therapy, and thyroid hormone therapy. However, a subset of patients develops resistance to radioiodine treatment, known as radioiodine-refractory DTC (rrDTC), presenting significant challenges in treatment. Over the past decade, significant advancements in understanding the molecular basis of thyroid cancer have led to the development and clinical adoption of tyrosine kinase inhibitors (TKIs) as a crucial treatment strategy for advanced disease stages. This overview examines the use of TKIs, specifically Lenvatinib, Sorafenib, and Cabozantinib, highlighting their effectiveness in halting cancer progression and managing symptoms. Nonetheless, the successful management of TKIs requires careful attention to their associated side effects, which is critical for maximizing treatment benefits and extending patient survival. Common adverse events (AEs) associated with TKI therapy include hepatic impairment, gastrointestinal issues, hypertension, proteinuria, hand-foot skin reaction, and fatigue, which typically manifest within several weeks of initiating treatment and significantly impact patient adherence to the therapy. Furthermore, the emergence of tumor-agnostic therapies marks a significant advancement in precision medicine, offering a more personalized treatment approach by targeting genetic mutations rather than the cancer's location. By exploring current research and clinical findings, we demonstrate the potential of TKIs to transform the therapeutic landscape for advanced thyroid cancer and offer insights into clinical practice.

Personalized management for medullary thyroid cancer

甲狀腺髓質癌的個人化醫療

Chun-Yu Liu
劉峻宇
Division of Medical Oncology, Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
臺北榮民總醫院 腫瘤醫學部 腫瘤內科

Medullary thyroid cancer (MTC) represents a rare but clinically significant malignancy originating from the parafollicular C cells of the thyroid gland. Unlike other types of thyroid cancer, MTC often presents therapeutic challenges due to its resistance to conventional treatments such as radioiodine therapy. However, recent advancements in personalized medicine have provided new avenues for tailored approaches in managing MTC patients.

This review explores the landscape of personalized treatment strategies for MTC, encompassing molecular profiling, targeted therapies, immunotherapy, and emerging modalities such as peptide receptor radionuclide therapy (PRRT). Through the identification of specific genetic mutations, particularly mutations in the RET proto-oncogene, and the development of novel agents targeting pathways implicated in MTC pathogenesis, personalized treatment regimens offer promising prospects for improved outcomes and enhanced quality of life for patients with MTC. Additionally, the integration of multimodal approaches including surgery, systemic therapy, and precision radiotherapy holds potential for synergistic effects in disease management.

Despite these advancements, challenges remain, including the optimization of treatment sequencing, the management of treatment-related toxicities, and the identification of reliable predictive biomarkers. Future directions in MTC research aim to refine personalized treatment algorithms, enhance therapeutic efficacy, and ultimately transform the management paradigm for this complex malignancy.

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2024兒童脊柱側彎照護、當代影像技術與轉譯研究

Image Can Help: Pediatric Scoliosis Care 2024 Current Techs and Translation Research

時 間：113年6月22日 08:30-12:00

Time：June 22, 2024 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 8&9, Chih-Teh Building
Taipei Veterans General Hospital

2024兒童脊柱側彎照護、當代影像技術與轉譯研究
Image Can Help: Pediatric Scoliosis Care 2024 Current Techs and Translation Research

Pediatric scoliosis care: Current trends and unmet needs in Taiwan

兒童脊柱側彎照護：趨勢及在台灣未滿足的需求

Chi-Kuang Feng

奉季光

Department of Orthopaedic and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 骨科部

Multidisciplinary Management of Pediatric Scoliosis

Pediatric scoliosis, especially early-onset scoliosis, requires a collaborative approach involving multiple specialties. Drawing on recent experiences from Europe and America, treatments are divided into non-surgical and surgical interventions.

Non-Surgical Treatment

Key non-surgical treatments encompass rehabilitation therapy, early intervention programs, nutrition, bone strengthening, enhancement of respiratory and cardiopulmonary functions, and management of associated conditions. These components are vital for comprehensive patient care.

Surgical Treatment

Surgical approaches are categorized into fusion and non-fusion corrective procedures. Non-fusion strategies involve implants that induce growth or extend the spine, controlling scoliosis progression while allowing normal growth.

Assessment Techniques

Before treatment, physical assessments are supplemented by medical imaging. The use of three-dimensional ultrasound to assess spinal curvature angles is increasingly popular, due to its ability to reduce radiation exposure. However, the limitations of ultrasound include the lack of axial images and the time-intensive nature of 3D ultrasound techniques. Innovations like zero echo time MRI and digital moiré projection contouring are being explored to overcome these challenges.

Rehabilitative Therapy

Rehabilitative exercise therapy is a highly specialized, patient-tailored treatment. The development of rehabilitation professionals and the use of technology to increase service capacity are promising. Technologies that present common exercises through virtual reality could enhance home accessibility for patients, making daily treatment more feasible.

Surgical Training and Innovation

The traditional apprenticeship in surgical training requires extensive learning. Advances in three-dimensional imaging and realistic 3D printing aids are enhancing surgical quality and accelerating skill transfer. This progress is crucial in surgical education, especially for complex and rare conditions.

Non-radiation measurement of cobb angle via fringe projection profilometry

無幅射數位條紋投影輪廓術來量測脊柱側彎角度

Cheng-Yang Liu
劉承揚
Department of Biomedical Engineering ,National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC
國立陽明交通大學 生物醫學暨工程學院 生物醫學工程研究所

Background: Adolescent idiopathic scoliosis (AIS) is a common spinal deformity in individuals aged ten and above, characterized by unknown etiology, resulting in spinal curvature and asymmetric trunk. Symptoms may include postural asymmetry, uneven shoulder height, and pelvic imbalance. Early diagnosis and treatment are crucial, involving physical therapy, orthotic bracing, and surgery, depending on severity and patient conditions. Early diagnostic methods include school screenings, Scoliometer, X-rays, and MRI/CT scans. However, despite being quick, the former two often yield judgment errors, with Scoliometer showing a correlation coefficient of 0.677 with Cobb angles. X-ray remains the most widely used despite radiation exposure concerns, while MRI and CT are more accurate but time-consuming and costly.

Methods: Our study employs fringe projection profilometry (FPP) using a projector to cast a known pattern onto the surface of the subject's back. A camera then captures images of the back with the superimposed pattern. These images serve as input data for a convolutional neural network (CNN), which outputs the Cobb angle and identifies the location and direction of scoliosis. We aim to establish an imaging system combined with a deep learning model to dynamically measure the morphology of the human back for clinical evaluation of scoliosis.

Results: Collaborating with Dr. Chi-Kuang Feng from the Taipei Veterans General Hospital, we recruited 147 participants for clinical trials. Our system takes only 1 ± 0.03 seconds to complete measurements with an ROI size of 1280 x 720, achieving 90 % accuracy in angle prediction and 75 % in location prediction. Biostatistical analysis indicates the effective angle range of our study is between 10 - 25 degrees, with 47 samples within this range, showing a discrepancy of ± 3.01 degrees from the gold standard, confirming the system's clinical value.

Conclusion: While currently a cross-sectional study, limiting its application to all scoliosis populations, the preliminary results demonstrate that our developed system can quickly and accurately assess scoliosis with clinical diagnostic value. We plan to continue patient recruitment in hospitals and refine the system, aiming for eventual medical device market approval to enhance public health.

AR/VR for scoliosis specific exercise training-pilot study

擴增 / 虛擬實境輔助脊椎側彎運動訓練的前驅研究

Wei-Chun Hsu

許維君

Science and Technology Graduate Institute of Biomedical Engineering ,National Taiwan University, Taipei, Taiwan, ROC

國立臺灣科技大學 醫學工程研究所

The statistics revealed that 3~5% of 11~16-year-old adolescents suffer from idiopathic scoliosis. The literature points out that patients with scoliosis have dysfunctions such as autonomic nerves, proprioception, and balance control, as well as asymmetric weight bearing of the lower limbs and abnormal gait pattern. Clinically, back brace and rehabilitation exercises are used to improve or prevent the deterioration of the spine curvature angle, so as to maintain the patient's quality of life and avoid surgical operations. Studies showed that the 3 months exercise program can improve the endurance of the back muscles and correct the curvature of the spine, thereby improving its dynamic posture control and balance ability. However, our research team has concluded that in Cobb's angle correction, C type has a significant effect, but S type seems no improvement. Is it because the Chinese people have insufficient exercise time and impractical training movements, resulting in poor efficiency? How to quantify the exercise time, guide the correct posture, and exercise intensity to achieve the best individualized effect?

Therefore, the proposed research direction is to develop a virtual reality core muscles interactive exercise game focusing on the training of the trunk core muscle group and the asymmetrical limbs guidance training of different hands and feet, and strengthen its vision, vestibule, and proprioception. The developing exercise is compared with method adopted in the clinics. At present, the physical therapist with a Schroth certificate in the rehabilitation department of Taipei Veterans General Hospital has confirmed the selected actions many times, and has observed and learned the scoliosis correction course of the therapist. The animation 3D software Blender has been used to make brief rehabilitation actions.

Exercise can strengthen the muscle strength of the trunk and lower limbs in patients with scoliosis, and improve their dynamic posture control and balance ability; but in the Cobb's angle correction, the S-type patients do not improve or even worsen. The virtual reality core muscle group interactive game, based on the training method, focuses on the training of the torso core muscles and the asymmetrical limbs guidance training of different hands and feet. It strengthens the interactive integration of vision, vestibule and proprioception somatosensory , and can guide the correct exercise posture to improve the asymmetric core muscles on both sides of the spine, control or reduce the Cobb's Angle in patients with S-scoliosis.

Virtual surgical planning and 3D printing for pediatric scoliosis

兒童脊椎側彎虛擬手術規劃與 3D 列印

Wun-Chan Yu

俞文展

3D Printing Technology and Resource Integration Center, Department of Medical Engineering, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Department of Biomedical Imaging and Radiological Sciences, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 醫學工程部 3D 列印技術發展暨資源整合中心

國立陽明交通大學 生物醫學影像暨放射科學系

Background: Pedicle screw insertion in scoliosis correction is challenging, especially for the pediatric cases. The spinal deformities and undersized pedicle diameter increase the risk of pedicle breach, which may cause spinal cord injury. To reduce the uncertainty, several surgical guidance techniques have been introduced in the past decades. Thanks to the avoidance of intraoperative radiation and ,in contrast to surgical navigation, the more affordable expenditure for patients and hospitals, virtual surgical planning (VSP) and 3D printed surgical guide (3DP SG) have become one of the promising guidance techniques over the past decade.

Methods: The optimal pedicle screw trajectory was planned in 3D Slicer, the medical image computing platform, according to spine CT images of scoliosis patients. The planned trajectory was inspected in axial, sagittal and coronal planes, ensuring no pedicle breach. Subsequently, patient-specific surgical guides, designed according to vertebral contour and planned trajectory, were materialized using a stereolithography 3D printer with biocompatible resin. Finally, the scoliotic spine models were 3D printed in order to confirm the stability of surgical guide when mounting on the spine.

Results: Nine pediatric scoliosis cases were enrolled in our experiment in 2023. The surgical planning and 3D printing workflow were established and fine-tuned based on the CT images and 3D printed scoliotic spine. The perfect fit between the surgical guide and vertebrae assisted surgeons in reducing the uncertainty of insertion trajectory. In a small portion of pedicles, unexpected trajectory inaccuracy was observed under the X-ray. Since the planned trajectories had been reconfirmed, the error must have been contributed by the post-VSP processes, such as foot plate design or deformation during 3D printing.

Conclusion: Virtual surgical planning and 3D printed surgical guide are beneficial for routine scoliosis correction operation in terms of uncertainty reduction, intraoperative radiation avoidance, and affordable expenditure. Identifying and improving the unexpected inaccuracy caused by post-VSP processes will be our next focus.

Bone Imaging with ZTE-MRI and its application to pediatric scoliosis

零回波時間磁共振造影技術：脊柱側彎骨骼應用

Chien-Yuan Lin

林建源

GE Healthcare, Taipei, Taiwan, ROC

美商奇異醫療

Magnetic resonance imaging (MRI) can non-invasively assess the proton pool and therefore provide excellent contrast of soft tissues, but has traditionally failed to visualize cortical bone due to its low proton density and rapid signal decay in transverse relaxation time (T2* ~ 0.4 ms). A newly-proposed three-dimensional (3D) zero-echo time (ZTE) MRI sequence utilizes a hard pulse excitation immediately followed by 3D radial k-space encoding to achieve a nominal echo time of zero, allowing for the visualization of the full transverse spin of cortical bone.

ZTE-MRI, offering the advantage of non-ionizing radiation, has been increasingly used for the evaluation of bone in various anatomical regions, including the cranium, extremities, sacroiliac joint, and spine. However, the application of this technique and the quality of whole-spine imaging remain largely unknown.

Scoliosis is a multifactorial 3D spinal deformity that requires continuous radiation-based follow-up of spinal curvatures using X-ray or CT, particularly in the pediatric population, for diagnosis and surgical planning. Radiation-free ZTE-MRI could provide an alternative solution for the evaluation of scoliosis.

This presentation will cover the physics of ZTE-MRI and its application for the assessment of 3D spinal deformity in pediatric scoliosis patients.

Rapid image annotation and analysis with interactive deep learning for medical image

互動式深度學習醫學影像快速圈選與分析

Gen-Jia Li
李根嘉
Chingyeh Corp., Ltd.
擎曄有限公司

This presentation explores rapid image annotation and analysis with interactive deep learning for medical images, beginning with an overview of key artificial intelligence (AI) models that have significantly impacted various fields. It covers ChatGPT for advanced natural language processing, Google Translate for language translation via deep learning, and the Transformer model, which is pivotal for text and image processing. The Vision Transformer (ViT) is highlighted for its application in image recognition, while Generative Adversarial Networks (GANs), particularly Pix2Pix, are discussed for their role in high-quality image generation.

Next, the presentation delves into the Amira software, a powerful tool for medical image analysis. Amira's integration of machine learning enhances its image processing capabilities. The presentation introduces Amira's new interactive AI segmentation tool, which allows for precise and efficient image annotation. Noise2Void, an unsupervised deep learning technique within Amira, is explained for its ability to denoise images without requiring clean reference images. Additionally, Amira's support for deep learning models facilitates both semantic and instance segmentation, crucial for detailed medical image analysis.

The advanced features of Amira-Avizo software are then explored, emphasizing its comprehensive 3D visualization and data analysis capabilities. A custom-developed iterative buds-growing neural network within Amira/Avizo is introduced, showcasing its ability to improve segmentation accuracy through iterative learning. Practical applications and case studies are presented to demonstrate the real-world benefits of these advanced tools in medical imaging, highlighting improvements in diagnostic accuracy and research outcomes.

In conclusion, the presentation summarizes the significant points discussed, reinforcing the importance of advanced AI models and tools in medical image analysis. Future trends and potential developments in AI for medical imaging are considered, emphasizing areas for further research and innovation.

「醫學研究論文獎」及
「盧致德院長獎」論文摘要

「盧致德院長獎」
(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院長獎)

「醫學研究論文獎」及「盧致德院長獎」論文摘要

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Performance of ChatGPT on the pharmacist licensing examination in Taiwan

Ying-Mei Wang[a,b,c], Hung-Wei Shen[b], Tzeng-Ji Chen[d,e,f,*]

[a] Department of Medical Education and Research, Taipei Veterans General Hospital Hsinchu Branch, Hsinchu, Taiwan, ROC; [b]Department of Pharmacy, Taipei Veterans General Hospital Hsinchu Branch, Hsinchu, Taiwan, ROC; [c]School of Medicine, National Tsing Hua University, Hsinchu, Taiwan, ROC; [d]Department of Family Medicine, Taipei Veterans General Hospital Hsinchu Branch, Hsinchu, Taiwan, ROC; [e]Department of Family Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [f]Department of Post-Baccalaureate Medicine, National Chung Hsing University, Taichung, Taiwan, ROC

Abstract

Background. ChatGPT is an artificial intelligence model trained for conversations. ChatGPT has been widely applied in general medical education and cardiology, but its application in pharmacy has been lacking. This study examined the accuracy of ChatGPT on the Taiwanese Pharmacist Licensing Examination and investigated its potential role in pharmacy education.

Methods. ChatGPT was used on the first Taiwanese Pharmacist Licensing Examination in 2023 in Mandarin and English. The questions were entered manually one by one. Graphical questions, chemical formulae, and tables were excluded. Textual ques- tions were scored according to the number of correct answers. Chart question scores were determined by multiplying the number and the correct rate of text questions. This study was conducted from March 5 to March 10, 2023, by using ChatGPT 3.5.

Results. The correct rate of ChatGPT in Chinese and English questions was 54.4% and 56.9% in the first stage, and 53.8% and 67.6% in the second stage. On the Chinese test, only pharmacology and pharmacochemistry sections received passing scores. The English test scores were higher than the Chinese test scores across all subjects and were significantly higher in dispensing pharmacy and clinical pharmacy as well as therapeutics.

Conclusion. ChatGPT 3.5 failed the Taiwanese Pharmacist Licensing Examination. Although it is not able to pass the examination, it can be improved quickly through deep learning. It reminds us that we should not only use multiple-choice questions to assess a phar- macist's ability, but also use more variety of evaluations in the future. Pharmacy education should be changed in line with the examina- tion, and students must be able to use AI technology for self-learning. More importantly, we need to help students develop humanistic qualities and strengthen their ability to interact with patients, so that they can become warm-hearted healthcare professionals.

Keywords. Artificial intelligence; ChatGPT; Educational measurement; Pharmacists; Pharmacy licensure

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Dual angiotensin receptor and neprilysin inhibitor reduced portal pressure through peripheral vasodilatation and decreasing systemic arterial pressure in cirrhotic rats

Chon Kit Pun[a,b], Ching-Chih Chang[a,c], Chiao-Lin Chuang[a,d], Hui-Chun Huang[a,b,*], Shao-Jung Hsu[a,b,*], Yi-Hsiang Huang[a,b], Ming-Chih Hou[a,b], Fa-Yauh Lee[a,b]

[a]Faculty of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [b]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [c]Division of Holistic and Multidisciplinary Medicine, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [d]Division of General Medicine, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background. Portal hypertension develops along with the progression of liver cirrhosis. Natriuretic peptides have been shown to reduce portal pressure but concomitantly activate the renin-angiotensin-aldosterone system (RAAS). Angiotensin receptor-nepri- lysin inhibitors (ARNIs) upregulate natriuretic peptides and avoid the adverse effects of RAAS activation. ARNIs have been shown to reduce portal pressure in rats with pre-hepatic portal hypertension, which involves relatively little liver injury. This study aimed to evaluate the relevant effects of an ARNI in rats with both liver cirrhosis and portal hypertension.

Methods. Male Sprague-Dawley rats received common bile duct ligation to induce liver cirrhosis and portal hypertension. Sham- operated rats served as surgical controls. All rats were randomly allocated into three groups to receive distilled water (vehicle), LCZ696 (an ARNI), or valsartan for 4 weeks. Portal hypertension and relevant derangements were assessed after treatment.

Results. Portal hypertension and hyperdynamic circulation developed in the cirrhotic rats. In the rats with cirrhosis and portal hypertension, both LCZ696 and valsartan reduced portal hypertension, mean arterial pressure, and systemic vascular resistance. The decrease in portal pressure was highly associated with the reduction in arterial pressure and systemic vascular resistance. Blood flow in hepatic, splanchnic, and portosystemic collateral systems was not altered. LCZ696 did not significantly influence liver injury or plasma cytokine levels. Liver fibrosis and splanchnic angiogenesis were not affected.

Conclusion. ARNI treatment exerted portal pressure lowering effects via peripheral vasodilatation and decreasing systemic arte- rial pressure in the rats with liver cirrhosis and portal hypertension. Caution should be taken when using ARNIs in liver cirrhosis.

Keywords. Angiogenesis; Angiotensin receptor-neprilysin inhibitor; Liver cirrhosis; Natriuretic peptide; Portal hypertension; Renin-angiotensin-aldosterone system

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Cell-free DNA as a prognostic and predictive biomarker in resectable distal common bile duct cancer

Bor-Shiuan Shyr, Shih-Chin Chen, Yi-Ming Shyr, Shin-E Wang, Bor-Uei Shyr*

Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, and National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Abstract

Background. Cell-free DNA (cfDNA) as an oncological biomarker has drawn much attention in recent years, but very limited effort has been made to investigate the prognostic values of cfDNA in distal common bile duct (CBD) cancer.

Methods. Plasma cfDNA was measured in 67 patients with resectable distal CBD cancer. Survival outcomes and the correlation of cfDNA with other conventional prognostic factors were determined.

Results. cfDNA levels were significantly higher in female patients, and those with poor tumor differentiation, abnormal serum car- cinoembryonic antigen (CEA) level, and stage III cancer. The significant prognostic factors included a high cfDNA level (>8955 cop- ies/mL), abnormal serum CEA level, stage III cancer, and positive resection margins. Compared with patients with high cfDNA level, those with lower cfDNA level (≤8955 copies/mL) had significantly better overall survival outcomes (74.4% vs 100% and 19.2% vs 52.6%, for 1- and 5-year survival rates, respectively, $p = 0.001$). The cfDNA level, perineural invasion, CEA level, and radicality were identified as independent prognostic factors for distal CBD cancer after multivariate analysis.

Conclusion. Circulating cfDNA levels play a significant role in predicting the prognosis and survival outcome for resectable distal CBD cancer. Furthermore, acting as a promising liquid biopsy, cfDNA could serve as a prognostic and predictive biomarker in combination with current conventional markers to improve diagnostic and prognostic efficacy.

Keywords. Biomarker; Cell-free DNA; Distal common bile duct; Prognosis

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Surgery for severe mitral regurgitation: The etiology matters

Yi-Lin Tsai[a,b], Ching-Wei Lee[b,c], Wei-Ming Huang[b,c,d], Hao-Min Cheng[b,c,d,e], Wen-Chung Yu[b,c], Chen-Huan Chen[b,d,e], Shih-Hsien Sung[c,d,f,*]

[a]Division of General Medicine, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Cardiovascular Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [c]Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [d]Institute of Public Health, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [e]Department of Medical Education, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [f]Institute of Emergency and Critical Care Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Abstract

Background. While surgery has been the standard treatment for patients with severe primary mitral regurgitation (PMR), the role of surgery for severe secondary mitral regurgitation (SMR) remained debated. We therefore investigated the prognostic differences of surgery for patients with either severe PMR or SMR.

Methods. Subjects hospitalized for heart failure were enrolled from 2002 to 2012. The severity of MR was assessed by continuity equation, and an effective regurgitant orifice area of ≥40 mm^2 was defined as severe. Long-term survival was then identified by the National Death Registry.

Results. A total of 1143 subjects (66.4 ± 16.6 years, 65% men, and 59.7% PMR) with severe MR were analyzed. Compared with PMR, patients with SMR were older, had more comorbidities, greater left atrial and ventricular diameter, and less left ventricular ejection fraction (all $p < 0.05$). While 47.8% of PMR patients received mitral valve surgery, only 6.9% of SMR patients did. Surgical intervention crudely was associated with 54% reduction of all-cause mortality in PMR (hazard ratio, 0.46; 95% confident interval, 0.32-0.67), and 48% in the subpopulation with SMR (0.52, 0.30-0.91). Propensity score matching analysis demonstrated the survival benefits of mitral valve surgery was observed in patients with PMR (log rank $p = 0.024$), but not with SMR. Among the unoperated subjects, age, renal function, and right ventricular systolic pressure were common risk factors of mortality, regardless of MR etiology.

Conclusion. Mitral valve surgery for patients with heart failure and severe MR was associated with better survival in patients with PMR, but not in those with SMR.

Keywords. Medical therapy; Severe mitral valve regurgitation; Surgery

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Risk factors for hemorrhagic complications following robotic-assisted partial nephrectomy

Cheng-Han Tsai[a], Hsiao-Jen Chung[a,b,*], Eric Y.H. Huang[a,b], Tzu-Ping Lin[a,b], Tzu-Hao Huang[a,b], William J. Huang[a,b]

[a]Department of Urology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Department of Urology, College of Medicine and Shu-Tien Urological Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Abstract

Background. The aim of this study was to analyze the risk factors for hemorrhagic complications in patients who underwent robotic-assisted partial nephrectomy.

Methods. We retrospectively reviewed the records of 260 patients who underwent robotic-assisted partial nephrectomy. Hemorrhagic complications were defined as bleeding, hematoma, or arteriovenous fistula requiring hemostatic medication, blood transfusion, or therapeutic intervention. Hemorrhagic complications were graded according to the modified Clavien classification system, and the hemorrhagic complication group comprised only those complications with Clavien grade II or higher. Thereafter, we investigated the presence of any relevant association between perioperative factors and hemorrhagic complications.

Results. Of 260 patients included in the study, 32 (12.3%) had hemorrhagic complications. The postoperative hemoglobin level was significantly lower in the hemorrhagic complication group than in the group without complications. The hemorrhagic compli- cation group had significantly more essential blood loss and a significantly longer length of hospital stay. In the univariate analysis, type 2 diabetes mellitus, Radius-scores tumor size as maximal diameter exophytic/endophytic properties of the tumor nearness of the deepest portion of the tumor to the collecting system or renal sinus anterior (a)/posterior (p) descriptor location relative to the polar line., sum of the renal size plus renal sinus involvement in the PADUA score is a simple anatomical system that can be used to predict the risk of surgical and medical perioperative complications in patients undergoing open NSS, prolonged console time (>180 minutes), prolonged warm ischemic time (>25 minutes), and method of pedicle control were statistically significant risk factors. In the multivariate logistic regression analysis, warm ischemic time >25 minutes was the only significant risk factor for hemorrhagic complications (odds ratio, 3.51; 95% confidence interval, 1.28-9.59; $p = 0.01$).

Conclusion. Patients who undergo robotic-assisted partial nephrectomy with a warm ischemic time >25 minutes are significantly more likely to have hemorrhagic complications and should hence receive careful perioperative follow-up.

Keywords. Arteriovenous fistula; Blood transfusion; Hemorrhage; Nephrectomy; Warm ischemia

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Cytotoxic T-lymphocyte antigen 4 polymorphisms and breast cancer susceptibility: Evidence from a meta-analysis

Hao-Yun Chang[a,b], Chao-Yu Liu[c], Yen-Li Lo[d], Shih-Hwa Chiou[e,f,g,h], Kai-Hsi Lu[i], Ming-Cheng Lee[j,*], Yuan-Hung Wang[k,l,*]

[a]School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, ROC; [b]Division of General Medicine, Department of Medical Education, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC; [c]Division of Traumatology, Department of Surgery, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC; [d]Institute of Biomedical Sciences, Academia Sinica, Nankang, Taipei, Taiwan, ROC.; [e]Institute of Pharmacology, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [f]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [g]Stem Cell & Genomic Center, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [h]Genomic Research Center, Academia Sinica, Taipei, Taiwan, ROC; [i]Department of Medical Research and Education, Cheng-Hsin General Hospital, Taipei, Taiwan, ROC; [j] Division of Infectious Diseases, Department of Internal Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan, ROC; [k] Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, ROC; [l]Department of Medical Research, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, ROC

Abstract

Background. Cytotoxic T-lymphocyte antigen 4 (CTLA-4) is an immune checkpoint and regulates the immune function of T cells. However, previous findings regarding the association of CTLA-4 polymorphisms and breast cancer remain inconclusive. Therefore, we performed a meta-analysis to investigate the potential effects of five polymorphisms (−1722 T/C, −1661 A/G −318 C/T, +49 A/G, and CT60 A/G) in the *CTLA-4* gene on breast cancer susceptibility.

Methods. Relevant literatures were systematically searched through electronic databases including PubMed, EMBASE, and Web of Science up to October 10, 2021. Available data were extracted and odds ratios (ORs) with 95% confidence intervals were used to estimate the pooling effect size. The Newcastle-Ottawa Scale was applied for assessing the quality of included studies. We conducted subgroup analyses based on ethnicity and control sources to explore levels of heterogeneity. Moreover, sensitivity analysis and publication bias were assessed.

Results. Finally, a total of 12 eligible studies regarding CTLA-4 polymorphisms and breast cancer were included. For overall analyses, only the +49 A/G polymorphism was significantly associated with breast cancer under allelic (OR = 1.19), dominant (OR = 1.27), and recessive (OR = 1.27) models. Ethnicity-based subgroup analysis found that the +49 A/G polymorphism has a significant risk (OR = 2.03) of breast cancer under the recessive model in the non-Asian population. Studies with hospital-based controls showed that the +49 A/G polymorphism has significant breast cancer risks under allelic (OR = 1.44), dominant (OR =

1.86), and recessive (OR = 1.60) models. In addition, those with population-based controls found that −1722 T/C polymorphism has a significant breast cancer risk under allelic (OR = 1.19) and dominant (OR = 1.26) models.

Conclusion. This meta-analysis suggested that CTLA-4 + 49 A/G polymorphism may significantly associate with breast cancer susceptibility. Future studies containing various populations are helpful for evaluating the impacts of CTLA-4 polymorphisms on breast cancer susceptibility.

Keywords. Breast cancer; Cytotoxic T-lymphocyte antigen 4; Immune checkpoint; Meta-analysis; Polymorphism

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Reduced-penetrance Huntington's disease- causing alleles with 39 CAG trinucleotide repeats could be a genetic factor of amyotrophic lateral sclerosis

Kang-Yang Jih[a,b,c], Kuan-Lin Lai[a,c,d], Kon-Ping Lin[a,c], Yi-Chu Liao[a,c,d], Yi-Chung Lee[a,c,d,*]

[a]Department of Neurology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Department of Physiology, National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan, ROC; [c]Department of Neurology, National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan, ROC; [d]Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

Abstract

Background. Expanded *HTT* alleles with 40 or more CAG repeats were recently found to be a rare cause of frontotemporal dementia and amyotrophic lateral sclerosis (ALS) spectrum diseases. The aim of this study was to investigate the role of *HTT* repeat expansions in a Taiwanese cohort with ALS.

Methods. We analyzed the numbers of CAG repeats in exon 1 of *HTT* in a cohort of 410 Taiwanese patients with ALS and 1514 control individuals by utilizing polymerase chain reaction and amplicon fragment length analysis.

Results. Only one of the 410 ALS patients carried a reduced-penetrance HD-causing allele with 39 CAG repeats, and none had an expanded *HTT* CAG repeats ≥40. The patient presented with rapidly progressive bulbar-onset ALS with disease onset at the age of 64 years. He had neither chorea nor cognitive impairment. He had a family history of chorea, but no other family member mani- fested with ALS. None of the 1514 control individuals carried an *HTT* expanded allele with CAG repeats larger than 37 repeats.

Conclusion. The *HTT* allele with 39 CAG repeats could be a genetic factor linked to ALS susceptibility.

Keywords. Amyotrophic lateral sclerosis; Huntington's disease; *HTT*; Polyglutamine expansion

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Immunoprofile of adenosquamous carcinoma in gastric cancer

Cheng-Han Wu[a], Cheng-Lun Lai[a], Chieh-Lin Jerry Teng[a,b,c,d], Wen-Liang Fang[e,f], Kuo-Hung Huang[e,f], Anna Fen-Yau Li[e,g], Hung-Yuan Yu[e,h,i], Nai-Jung Chiang[e,j], Yee Chao[e,j], Yi-Ping Hung[e,j,*], Ming-Huang Chen[e,j,*]

[a]Division of Hematology/Medical Oncology, Department of Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, ROC; [b]Department of Life Science, Tunghai University, Taichung, Taiwan, ROC; [c]School of Medicine, Chung Shan Medical University, Taichung, Taiwan, ROC; [d]College of Medicine, National Chung Hsing University, Taichung, Taiwan, ROC; [e]School of Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [f]Division of General Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [g]Department of Pathology, Cheng Hsin General Hospital, Taipei, Taiwan, ROC; [h]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [i]Hospitalist Ward, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [j]Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background. Gastric adenosquamous carcinoma (GASC) is a rare subtype of gastric cancer. Research on GASC treatment is limited, and its outcome is usually poor. We investigated the clinical features, immunoprofile of GASC, and determined the optimal treatment modality for these patients.

Methods. Patients with GASC from Taipei Veterans General Hospital were retrospectively reviewed. Clinical features and treat- ment outcomes were evaluated. Adequate samples were examined for surrogate biomarkers for immunotherapy by IHC staining.

Results. Total 14 (0.35%) GASC patients were found among 4034 gastric cancer patients. The median tumor size was 6.8 cm in 10 patients with stage III GASC, and all these patients underwent radical gastrectomy followed by adjuvant therapy. The median progression-free survival (PFS) and overall survival (OS) were 6.0 and 11.5 months, respectively. Two patients with stage IV GASC received frontline immunotherapy. Their median PFS and OS were 9.0 and 12.5 months. In immunoprofiling, 25.0% (n = 3), 75.0% (n = 9), and 33.3% (n = 4) of the samples had deficient mismatch repair (dMMR) protein, combined positive score (CPS) of ≥1, and CPS of ≥10, respectively. The univariate analysis revealed that programmed death-ligand 1 ≥5% (HR: 0.12; 95% CI: 0.01-0.97; $p = 0.047$) was significant associated with superior OS. One stage IV patient with CPS ≥10 and dMMR proteins received nivolumab monotherapy as frontline treatment that resulted 14-month PFS.

Conclusion. Patients with GASC are more likely to yield positive results for CPS and dMMR. Biomarkers should be examined, and immunotherapy can be considered as frontline systemic treatment.

Keywords. dMMR; Gastric adenosquamous cell carcinoma; Immune therapy; PDL1

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Radiomic features derived from pretherapeutic MRI predict chemoradiation response in locally advanced rectal cancer

Yen Chou[a,b], Szu-Hsiang Peng[c], Hsuan-Yin Lin[d], Tien-Li Lan[e], Jeng-Kae Jiang[f,g], Wen-Yih Liang[h,g], Yu-Wen Hu[e,g], Ling-Wei Wang[e,g,*]

[a]Department of Medical Imaging, Fu Jen Catholic University Hospital, New Taipei City, Taiwan, ROC; [b]School of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan, ROC; [c]Department of Medical Imaging, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC; [d]Division of Radiology, Taichung Veterans General Hospital, Taichung, Taiwan, ROC; [e]Division of Radiation Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [f]Division of Colorectal Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [g]School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [h]Department of Pathology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background: The standard treatment for locally advanced rectal cancer (LARC) is neoadjuvant concurrent chemoradiother- apy (CRT) followed by surgical excision. Current evidence suggests a favorable prognosis for those with pathological complete response (pCR), and surgery may be spared for them. We trained and validated regression models for CRT response prediction with selected radiomic features extracted from pretreatment magnetic resonance (MR) images to recruit potential candidates for this watch-and-wait strategy.

Methods: We retrospectively enrolled patients with LARC who underwent pre-CRT MR imaging between 2010 and 2019. Pathological complete response in surgical specimens after CRT was defined as the ground truth. Quantitative features derived from both unfiltered and filtered images were extracted from manually segmented region of interests on T2-weighted images and selected using variance threshold, univariate statistical tests, and cross-validation least absolute shrinkage and selection operator (Lasso) regression. Finally, a regression model using selected features with high coefficients was optimized and evaluated. Model performance was measured by classification accuracies and area under the receiver operating characteristic (AUROC).

Results: We extracted 1223 radiomic features from each MRI study of 133 enrolled patients. After tumor excision, 34 (26 %) of 133 patients had pCR in resected specimens. When 25 image-derived features were selected from univariate analysis, classifica- tion AUROC was 0.86 and 0.79 with the addition of six clinical features on the hold-out internal validation dataset. When 11 image- derived features were used, the optimized linear regression model had an AUROC value of 0.79 and 0.65 with the addition of six clinical features on the hold-out dataset. Among the radiomic features, texture features including gray level variance, strength, and cluster prominence had the highest coefficient by Lasso regression.

Conclusion: Radiomic features derived from pretreatment MR images demonstrated promising efficacy in predicting pCR after CRT. However, radiomic features combined with clinical features did not result in remarkable improvement in model performance.

Keywords: Chemoradiotherapy; Magnetic resonance imaging; Pathological complete response; Radiomics; Rectal cancer

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Gastrointestinal and liver manifestations in patients with COVID-19

I-Cheng Lee[a,b], Teh-Ia Huo[a,c,d,*], Yi-Hsiang Huang[a,b,e,*]

[a]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Faculty of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC; [c]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [d]Institute of Pharmacology, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC; [e]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC

Abstract

As the outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread over the world, the World Health Organization has declared the outbreak of COVID-19 an international public health emergency. Besides typical respiratory symptoms and signs of COVID-19, digestive symptoms and liver injury have been frequently reported during the course of the disease. In this review, we summarized the recent studies report- ing of gastrointestinal and liver manifestations during the course of COVID-19. Digestive symptoms, including anorexia, nausea, vomiting, and diarrhea, are not uncommon in patients with COVID-19, and in some cases digestive symptoms may occur in the absence of any respiratory symptoms. Furthermore, SARS-CoV-2 could be detected in the stool of infected patients, implicating the possibility of fecal–oral transmission. Attention should also be paid to monitor liver function during the course of COVID-19, especially in patients with higher disease severity.

Keywords: COVID-19; Digestive; Gastrointestinal; Liver; Severe acute respiratory syndrome coronavirus 2

銘謝贊助單位

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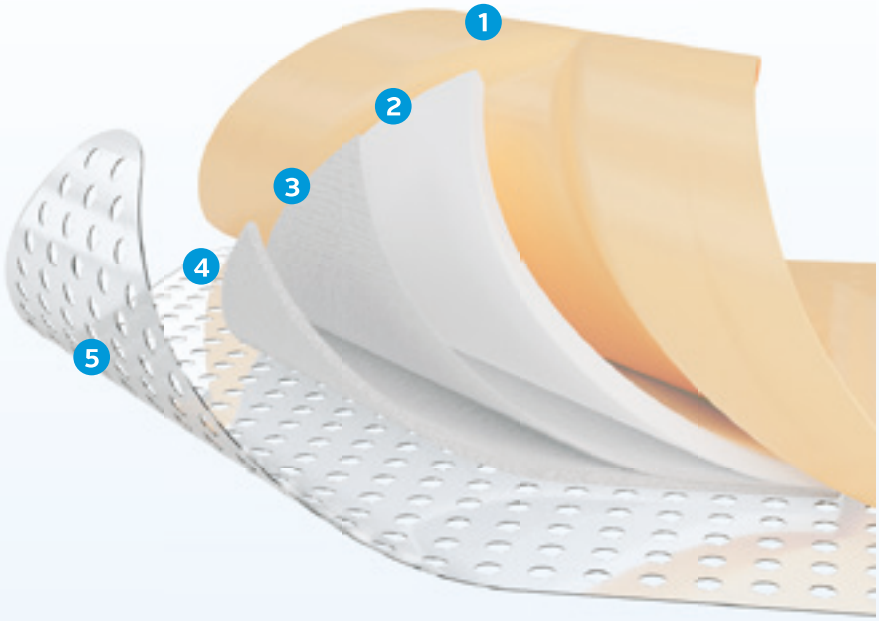

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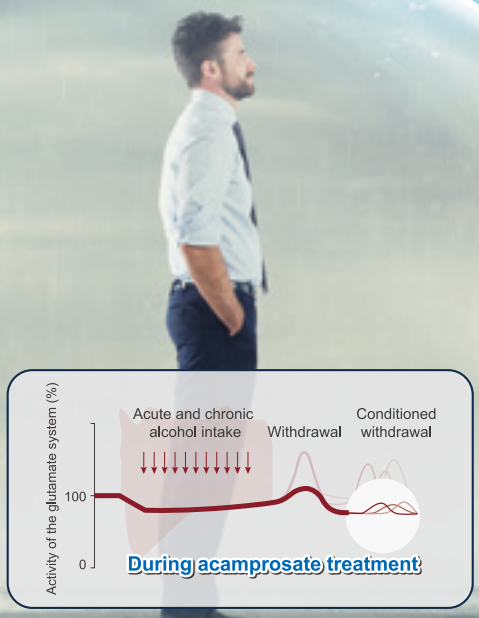

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1. Roche studies No. RD002542 and RD002543

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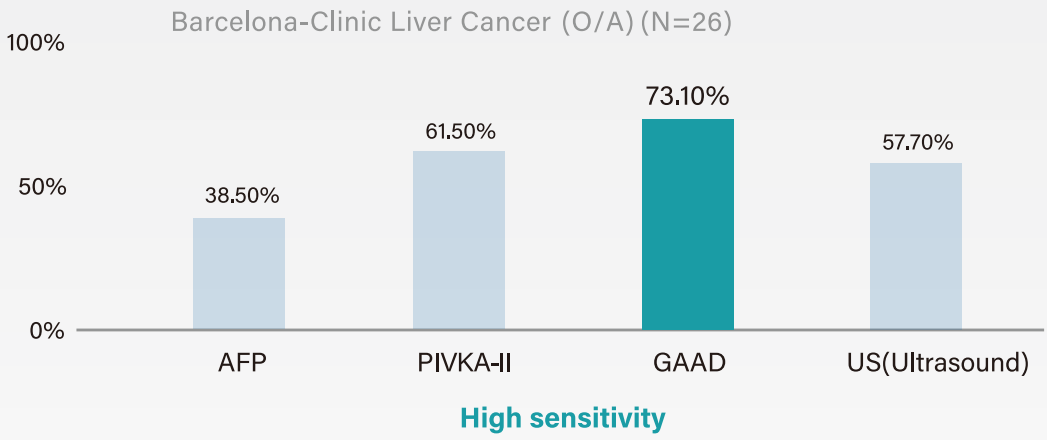

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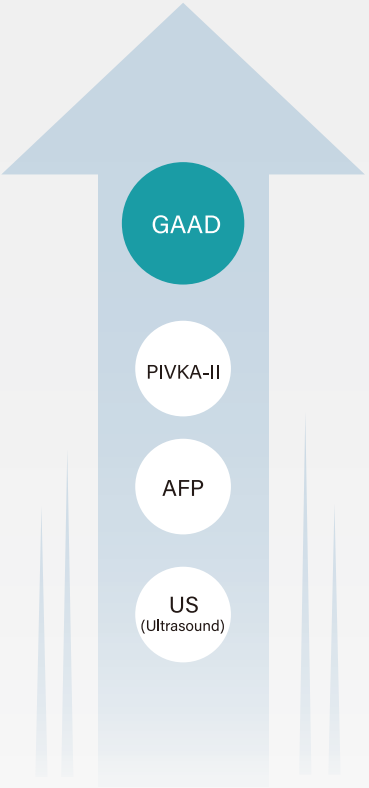

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6. The clinical utility of Elecsys GAAD score in the diagnosis of hepatocellular carcinoma, Ming-Lung Yu, APASL STC HCC 2022

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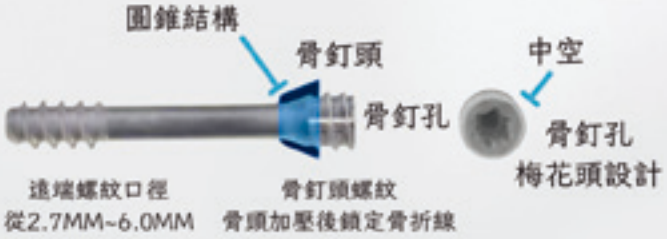

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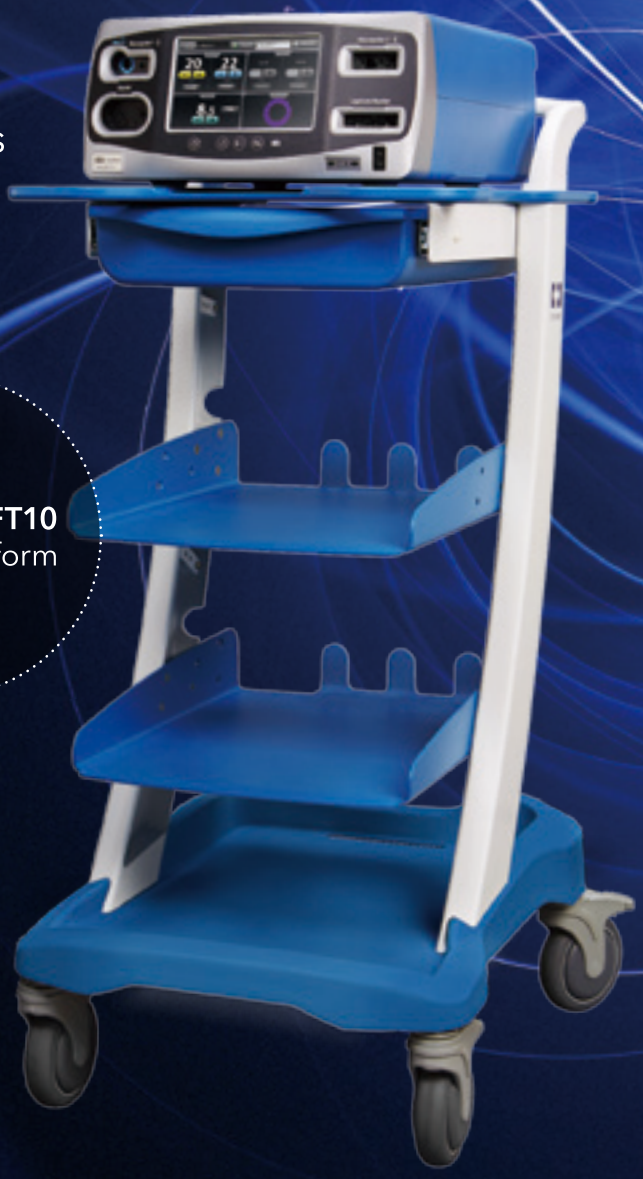

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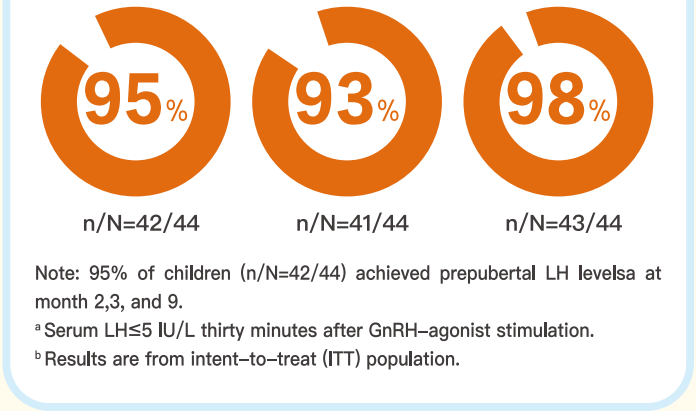


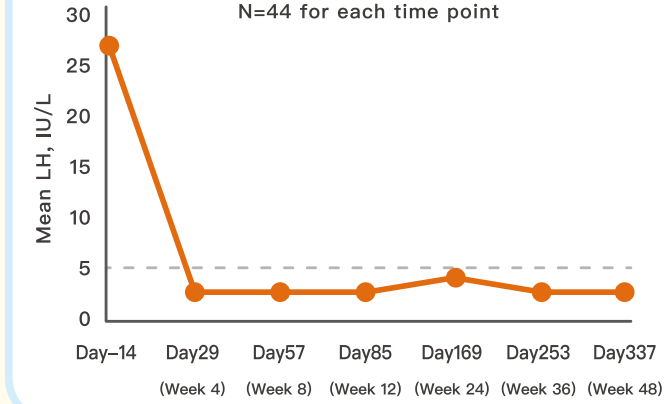
Note: 95% of children (n/N=42/44) achieved prepubertal LH levelsa at month 2,3, and 9.

[a] Serum LH≤5 IU/L thirty minutes after GnRH-agonist stimulation.

[b] Results are from intent-to-treat (ITT) population.

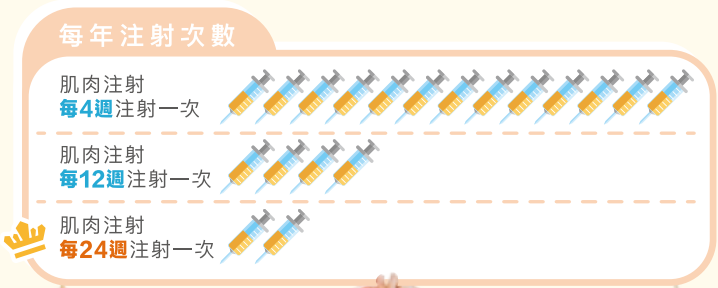
98%的受試者在持續用藥後12個月後，可有效控制 LH ≤5 IU/L

Pamorelin（Triptorelin）在用藥期間可有效降低 LH 濃度



在用藥之後，體內平均 LH 濃度控制在 5 IU/L以內

Reference: Karen Klein, et al. J Pediatr Endocrinol Metab. 2016, 29(11):1241-8.



帕摩霖長效注射劑 22.5 mg Pamorelin (Triptorelin pamoate)

適應症｜治療中樞性性早熟 (central precocious puberty, CPP) 發病年齡在 2 歲(含)以上至 8 歲前(女孩)或 9 歲前(男孩)之兒童。

禁忌症｜禁止用於已知對triptorelin或藥品中任何其他成分，或其他促性腺激素釋放素 (GnRH) 促進劑 或 GnRH 過敏的患者。

常見副作用｜月經 (陰道出血)。

本藥品需在醫師監督下投與，詳細資訊請參閱仿單。

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Debiopharm
PAM-2023-05-002

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60/30/15 mg 全劑量

提供心房顫動病人預防中風的安心理想選擇

- 有效預防中風及全身性栓塞發生[1、2、3]
- 顯著降低重大出血風險[1、3]
- 一天一次，簡單方便[3]

Lixiana® 劑量指引

標準劑量

Lixiana® 60 mg
一天一次

若合併 BCD 臨床因素

若符合下列任一項以上

- **Body Weight**
  ≦60 kg
- **CrCl**
  15~50 mL/min
- **Drug**
  併用 P 醣蛋白 (P-gp) 抑制劑 *1

Lixiana® 30 mg
一天一次

若為特殊族群

年紀 ≧80 歲 且 $CHADS_2$ score ≧2 分

並且符合下列任一項以上

- **重要器官出血史**
  (顱內 / 眼內 / 腸胃道出血)
- **Body Weight**
  ≦45 kg
- **CrCl**
  15 ≤ CrCl < 30 mL/min
- **長期使用 NSAIDs 或抗血小板藥物**

Lixiana® 15 mg
一天一次

根據 ELDERCARE-AF，因擔心出血風險而無法使用其他口服抗凝血劑之核准劑量，且病人符合上述條件，可以考慮此劑量。

1. Giugliano RP et al. N Engl J Med. 2013 Nov 28;369 (22):2093-104
2. Okumura K et al. N Engl J Med. 2020 Oct 29;383 (18):1735-1745.
3. Lixiana® Package insert.

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IN JUST
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Quickly deliver cure† with 8-week MAVIRET
so your patients‡ can move forward free from HCV.

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Clopidogrel
Polymorph Form 2

改善腦、心、周邊血管栓塞疾病

有效降低中風、急性冠心症、與周邊動脈栓塞的發生，值得醫師信賴

Broad Spectrum of Atherothrombosis Prevention.[1]

保栓通膜衣錠 75 毫克 PLAVIX Film-coated Tablets 75mg 每錠含 75mg Clopidogrel (hydrogen sulphate)

【適應症】適用於粥狀動脈栓塞事件的次級預防於下列病患：- 降低近期發生中風、心肌梗塞或周邊動脈血管疾病的粥狀動脈硬化病人之粥狀動脈栓塞事件 (如：心肌梗塞、中風或其他因血管病變引起的死亡) 的發生。- 與 aspirin 併用降低非 ST 段上升之急性冠心症 (不穩定性心絞痛和非 Q 波型心肌梗塞) 病人 (包括經皮冠狀動脈介入性治療後放置支架的患者) 之粥狀動脈栓塞事件。- 與 aspirin 併用可用於以內科治療的 ST 段上升之急性心肌梗塞病人。- 不適合接受 Vitamin K antagonists 的心房纖維顫動患者，併有至少一個發生血管事件危險因子，且屬於出血危險性低者，可與 aspirin 併用以預防粥狀動脈栓塞及血栓栓塞事件，包括中風。- 與 Aspirin 併用，適用於降低急性缺血性腦中風 (NIHSS 分數 ≤3) 或中度至高度風險暫時性腦缺血 (TIA) 病人之中風風險。**【用法用量】**成人和老年人：Clopidogrel 的建議劑量為每天 75mg，一天一次，可和食物同時服用或分開服用。有急性冠心症的病人：- 非 ST 段上升的急性冠心症 (不穩定性心絞痛或非 Q 波型心肌梗塞)：Clopidogrel 治療應從單一預載劑量 (loading dose) 300mg 或 600 mg 開始給藥。75 歲以下欲接受經皮冠狀動脈介入性治療的病人可考慮給予 600 mg 預載劑量，之後每天給予 clopidogrel 75mg，並同時服用乙醯水楊酸 (aspirin) 75mg- 325mg，一天一次。由於高劑量的 aspirin 可能引起出血的危險，建議 aspirin 的劑量不可超過 100mg。目前 clopidogrel 最適當的治療期尚未確立，臨床試驗數據可支持使用至 12 個月，最大效益約在服藥後第三個月出現。- ST 段上升之急性心肌梗塞：不論是否使用血栓溶解劑，clopidogrel 應給予每日單一劑量 75mg，開始時可給予或不給予預載劑量 (loading dose)，同時併用 aspirin。超過 75 歲的病人開始治療時，不應給予預載劑量。症狀發生後應儘早開始合併療法且應持續使用至少四個星期。併用 clopidogrel 與 aspirin 超過四個星期的效益尚未確立。患有心房纖維顫動的病人，clopidogrel 應給予每日單一劑量 75mg，aspirin (日劑量 75-100 mg) 應同時給藥並與 clopidogrel 持續併用治療之。急性缺血性腦中風 (NIHSS 分數 ≤3) 或中度至高度風險暫時性腦缺血 (TIA) 病人：Clopidogrel 與 Aspirin 併用治療：開始治療時，Clopidogrel 的預載劑量為單次口服 300mg，後續則每日口服一次 75mg；Aspirin 的劑量為每日口服一次 75-100mg。Clopidogrel 及 Aspirin 應在腦血管事件發生後 24 小時內盡早開始給藥並持續 21 天。在 Clopidogrel 與 Aspirin 並用治療結束時，需接續評估使用適當之單一抗血小板藥物 (antiplatelet agents) 作為缺血性腦中風之次級預防。藥物基因學：肝臟酵素 CYP2C19 代謝功能不佳病人會降低 clopidogrel 之抗血小板反應，雖然提高 clopidogrel 劑量會增強 CYP2C19 代謝功能不佳病人之抗血小板反應，惟 CYP2C19 代謝功能不佳病人之適當給藥劑量尚未完全建立。兒童：兒童及青少年之療效及安全性尚未建立。老年病人：年齡 ≥75 歲病人的預載劑量。腎臟功能不全之病人：使用於腎功能不良病人之經驗有限。肝臟功能不全之病人：使用於可能有出血體質的中度肝功能不良病人之經驗有限。**【禁忌】、對藥品主成份或其他非活性成份過敏者。、嚴重肝功能不良的患者。、正在出血的患者如消化性潰瘍或顱內出血的患者。、懷孕及授乳婦。【警語及注意事項】由於有血液學方面的不良反應和出血的危險，在治療期間應檢驗血球計數，且當出現有出血的臨床症狀時應立即進行適當的檢查 (請參考 "不良反應" 欄)。和其他抗血小板製劑一樣，clopidogrel 應小心使用於可能有出血危險的病人，例如：創傷、手術、其他病理狀況或接受 aspirin、肝素、glycoprotein IIb/IIIa 抑制劑、非固醇類抗炎止痛劑 (NSAID) 包括 Cox-2 抑制劑、或選擇性血清素再吸收抑制劑 (SSRIs) 或 CYP2C19 強效誘導劑或其他與出血風險有關的藥物。急性非心因性栓塞 (non-cardioembolic) 缺血性中風或暫時性腦缺血發作 (TIA) 的病人不建議使用三重抗血小板療法 (clopidogrel + aspirin + dipyridamole) 來預防二次中風，因為這會增加出血的風險。病人應小心注意任何可能的出血徵兆，包括隱匿性的出血，特別是在治療開始的第一週及手術或侵入性心臟檢查後。由於可能會增加出血的危險，clopidogrel 不建議與口服抗凝血劑併用。患有非 ST 段上升之急性冠心症且年齡 ≥75 歲的病人不建議使用 clopidogrel 600 mg 預載劑量，因為這方面的資料有限且會增加此族群的出血風險。【交互作用】與出血風險有關之藥物。口服抗凝血劑。Glycoprotein IIb/IIIa 抑制劑。乙醯水楊酸 (aspirin)：由於 clopidogrel 和 aspirin 併用產生藥效學上的交互作用是可能的，會導致出血的危險性增加，因此併用時應小心。肝素 (Heparin)。血栓溶解劑 (Thrombolytics)。非固醇類抗炎止痛劑 (NSAIDs)。選擇性血清素再吸收抑制劑 (SSRIs)。CYP2C19 的強效或中效抑制劑 /CYP2C19 強效誘導劑不鼓勵併用之。CYP2C8 的受質藥物 (repaglinide)。需同時給予嗎啡或其他鴉片類促效劑之急性冠心症病人，應考慮使用不經胃腸的抗血小板製劑。不建議抗反轉錄病毒治療 (ART) 增效劑與 clopidogrel 併用。【懷孕及哺乳】懷孕：由於資料不足，懷孕期間不建議使用 clopidogrel。哺乳：為謹慎起見接受 Plavix 治療時應停止授乳。【不良反應】常見 (≥1/100，<1/10)：血腫、鼻出血、胃腸道出血、腹瀉，腹痛，消化不良。瘀血。使用前請詳閱藥物說明書警語及注意事項。【過量】服用過量的 clopidogrel 會導致出血時間延長及其他出血的併發症。若發生出血應採取適當之治療，目前並未發現 clopidogrel 的解毒劑，若需要立即校正過長的出血時間，輸血小板可能可以校正 clopidogrel 的作用。【藥理特性】藥理治療分類：非 Heparin 之血小板凝集抑制劑 ATC Code: B01 AC/040

仿單版本 Ref. CCDS v30+32_17Feb2022 衛署藥輸字第 022932 號 簡易仿單版本日期：May-2023 藥商名稱：賽諾菲股份有限公司 藥商地址：台北市 11010 松仁路 3 號 7 樓

Reference
1. Plavix 仿單資訊 CCDS v30+32_17Feb2022.

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