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Scientific Tracks & Abstracts

(Day 1)

Tomoo Itoh et al., J Clin Exp Pathol 2016, 6:5(Suppl)
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Validation study of WSI based primary diagnosis by nine Japanese academic institutes

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Background: Several reports demonstrate the availability for the primary diagnosis done by digitized slide glass specimen with Whole Slide Imaging (WSI). However, there has been no publication of the validation study from Japan, which is the requirement to obtain approval by Japanese Pharmaceuticals and Medical Devices Agency (PMDA).

Objective: To provide evidence of usability of WSI diagnosis for primary diagnosis compared to conventional glass slide diagnosis by multicenter consortium.

Method: 900 cases, 1070 slides available for histopathologic diagnosis by H&E observation in nine hospitals. The slide glasses were digitized and independent pathologists trained based on CAP guidelines had reviewed and made diagnosis for the digitized cases. Digitization was performed by 20x or 40x optical magnifications utilizing whole slide imaging scanner in each institute and observers reviewed conventional glass slides after more than 2 weeks of washout time interval. Discrepancies between microscope slide and WSI diagnosis were classified into 3 categories; concordance, major discrepancy (defined as ones associated with significant difference in clinical treatment) and minor discrepancy (defined as ones associated with no significant difference in clinical treatment). All pathologists were gathered to review cases with discrepant diagnosis and voted to decide category and cause of discrepancy.

Result: There were 9 diagnoses with major discrepancy (0.8%) and 38 minor diagnoses with discrepancy (3.6%) between WSI and microscopic diagnosis. Eight among 9 diagnoses with major discrepancy were judged as proper to the diagnoses based on conventional microscopic observation. There was no association between level of discrepancy and categories of organ, collecting method or digitized optical magnification. Major discrepancy rates in all institutes were almost similar ranged from 0% to 3.0%.

Conclusion: Our results indicate the safety and efficacy of WSI based primary diagnosis for cases with biopsy and small surgery in Japan. We also emphasize the need of intense training specified for digital pathology diagnosis before its recruitment to the routine clinic.

Biography

Tomoo itoh has completed his PhD at Hokkaido University Graduate School of Medicine and presently he is a Professor and Deputy Director of Diagnostic Pathology at Kobe University Hospital, Japan. He is a board certified Member of the Japanese Society of Pathology and board certified Member of the Japanese Society of Clinical Cytology. He has published more than 34 papers in reputed journals.

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Notes:

Ichiro Mori et al., J Clin Exp Pathol 2016, 6:5(Suppl)
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Trials of international WSI telepathology consultation with eastern Asian countries

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Using digital pathology, we made several trials of international WSI (Whole Slide Imaging) telepathology consultation with eastern Asian countries. In eastern Asia, there is big difference of infrastructures between countries. This work is supported by Japanese Ministry of Economy, Trade and Industry. We set up a consortium with Hamamatsu photonics for WSI scanner, Sakura Finetek for pathology equipment, Toshiba Medical Systems for radiological images and Panasonic System Solutions for Network and TV conference system. We mainly tried real time online teleconference using WSI images. In particular, we prepared interesting cases prior the teleconference, scan to WSI and stored in the server. Attended pathologists observed these WSIs before the teleconference, make diagnosis and leave the diagnosis document to the server. One of our members visited to their hospitals and he moderate the teleconference. Discussion through teleconference system was made in English. The WSI images maintained adequate quality for pathology diagnosis even looked from abroad. The diagnoses matched well between hospitals. The response of WSI viewer depended on the web speed. Infrastructure including Web speed was differed between countries. When we shared band width to the teleconference system or radiological images sent in the background, the response deteriorates and was not good enough for diagnosis. It was confirmed that there is no problem in international remote diagnosis using WSI. The international WSI telepathology diagnosis is now in a stage of practical use. Remaining issues are language, quality of glass slides, difference in diagnosis criteria, economical and responsibility issues, etc. Finally, based on these experiments, we came to agreement with Vietnamese Government and decide to open a multiphasic health check facility in Ho-Chi-Minh city, Vietnam.

Biography

Ichiro Mori has completed his PhD from Gunma University and Postdoctoral studies from Tokai University School of Medicine. He is a Professor of Pathology, Mita Hospital, International University of Health and Welfare. He has published more than 25 papers in reputed journals.

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Michael Grunkin, J Clin Exp Pathol 2016, 6:5(Suppl)
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A business case for quantitative digital pathology

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Pathologists all over the developed world are increasingly challenged both by the growing diagnostic volume and the complexity of cases to be read. These challenges are further amplified by shrinking budgets and the competitive pressures from new diagnostic modalities such as gene expression assays and next-generation sequencing. The widely published lack of data quality in terms of reproducibility, sensitivity and specificity of manual readings has probably contributed to generating a growing demand for new diagnostic modalities and probably also contributed to the growing pressure on budgets. Image analysis has the potential to impact significantly on data quality. In order to have such an impact, a number of essential technical solution components are required for mitigating several error sources on the journey from biopsy to diagnostic, prognostic or predictive tissue data. Solution requirements include: Correct and verifiable identification of invasive tumor cells, excluding stromal and pre-invasive cells, handling of tumor heterogeneity and identification of hot-spots, standardized quantification of sub-cellular biomarkers and gene probe assays in tumor cells and assessment of staining quality, which at least is possible for immunohistochemical markers. In studies, evidence is found suggesting that these four solution components have a profound impact on data quality. These studies further indicate that the combination of immunohistochemistry with image analysis controls are capable of yielding data of a quality and clinical utility which is at least comparable to alternative and competing methods but at a significantly lower cost. The underlying technical solution components and clinical study results are presented.

Biography

Michael Grunkin is the CEO of Visiopharm A/S, Denmark. He has obtained his PhD in Image Analysis and Spatial Statistics from the Technical University of Denmark in 1993. His Post-doctoral work at Massachusetts Institute of Technology and Harvard Medical School was focused on the application of image analysis for medical devices. From 1996, he was the technical Founder of two Danish medical device companies based on image analysis as the platform technology. In 2001, he has Co-Founded Visiopharm A/S, which is a quantitative digital pathology company with focus on cancer research, diagnostics and the general standardization of tissue data.

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Notes:

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Biomarkers for breast cancer: Where we are now

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Breast cancer is one of the leading causes of cancer death in women, but there has been a sustained decline in mortality rates over the last decades despite the increasing incidence of breast cancer. The effective adjuvant systemic treatment is one of the major contributors to this recent development. Breast cancer treatment has experienced several changes in the past decades due to the discovery of specific prognostic and predictive biomarkers that enable targeted therapies. In addition to the classical clinical prognostic factors of breast cancer, established biomarkers such as estrogen receptor and progesterone receptor have played a significant role in the selection of patients benefiting from endocrine therapy. More recently, the human epidermal growth factor receptor 2 (HER2) has been validated to be not only a prognostic factor, but also a predictor of response to HER2 targeting therapy. The marker of proliferation Ki67 has recently emerged as an important marker due to several applications in neoadjuvant therapy in addition to its moderate prognostic value. In the past two decades, the human genome project and the development of high-throughput technologies prompts the rapid emerging multi-gene signature for certain tumors with characteristic clinical behaviors to novel therapy strategies. The gene expression profiling of tumors allows the measurement of thousands of mRNA transcripts in one single experiment using DNA microarrays. In combination of rapidly developing bioinformatics technology, the novel multi-gene signatures play an increasingly important role in patient care. It is imperative for the practicing pathologists to keep updated knowledge of new development of biomarkers, the biological scenario of the development and their potential clinical applications.

Biography

Hong Amy Zhang is currently an Associate Professor in the Department of Pathology and Translational Molecular Pathology in University of Texas-MD Anderson Cancer Center in Houston, TX, specializing in Breast Cancer Pathology. Prior to joining UT-MDACC, she was an Assistant Professor in the Department of Pathology in the Baylor College of Medicine from 2006 to 2009. She is an American board certified practicing Pathologist since 2003. She has expertise in diagnosing breast cancers and the interpretation of the biomarkers relevant to breast cancers for patient care. She is also actively supervising research scientists and trainees on translational and laboratory research, focusing on the characterization of tumor markers significant for breast tumorigenesis and the development of small molecule inhibitors and potential novel molecular targets for breast cancer treatment.

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David A Gutman, J Clin Exp Pathol 2016, 6:5(Suppl)
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The cancer digital slide archive (CDSA): A web based resource linking pathology, radiology and genomics

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The Cancer Genome Atlas (TCGA) is an NCI funded project integrating clinical, histopathological, molecular (mRNA/miRNA, protein, copy number, etc) and metadata for over 25 different cancer types. The overall goal is to harness large data sets to discover insights in cancer progression. Several recent TCGA studies have illustrated important relationships between morphology observed in whole-slide images, clinical data and genetic events and therefore the ability to link these data sources over hundreds of patients could potentially lead to a greater insight in cancer progression. However, the integration and visualization is a common challenge in biomedical informatics and better tools are needed to combine the vast and disparate data types. Our group has developed a number of web-based tools to support the federation, visualization and analysis of both pathology and radiology imaging data. The CDSA houses over 25000 digital pathology images as well as integrated tools to view related metadata, as well as for image markup and data analysis. A brief overview of some of the capabilities and data available in this public resource will be discussed. In addition, we will review some of the open-source tools used to power this archive. Finally, some of the science that this technology has enabled will be reviewed.

Biography

David A Gutman has received his MD/PhD from Emory University and then completed a Psychiatry Residency. He has published over 75 papers and has a broad range of interests in the digital imaging (radiology and pathology) and clinical informatics. He is currently an Assistant Professor of Neurology, Psychiatry & Biomedical Informatics and is also a Staff Physician at the Atlanta VA.

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HistomicsTK: Developing an open-sourced platform for integrated histopathology analysis

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Open-sourced software is an important resource for research communities, providing transparency, reproducibility and enabling broad engagement among researchers to understand and build upon the communities' work. While mature open-sourced image analysis tools are commonplace in the radiology domain, the digital pathology domain has relatively few open source tools for histopathology image analysis. This talk will discuss ongoing efforts by Emory and Kitware, Inc. to develop HistomicsTK, an open source platform for histopathology image analysis. HistomicsTK enables users to analyze large collections of whole-slide images, providing algorithms for common image analysis tasks including segmentation, feature extraction and classification. It provides infrastructure for the parallel execution of image analysis pipelines and enables algorithm/pipeline portability and easy deployment using containerization technology and network-based access to computational capabilities through REST interfaces. Case studies using HistomicsTK and its precursor tools will be presented including systems for interactive classification, nuclear morphometrics and immunohistochemical quantification. Using data from The Cancer Genome Atlas we will demonstrate how HistomicsTK can used to analyze multifaceted datasets containing digital pathology images and comprehensive genomic and clinical characterizations of cancers to explore prognostic imaging biomarkers and to investigate fundamental disease processes like angiogenesis and lymphocytic infiltration.

Biography

Lee Cooper is an Assistant Professor with joint appointments in Biomedical Informatics and Biomedical Engineering at Emory University and Georgia Tech. He has received his PhD degree in Electrical Engineering from Ohio State University in 2009 and then joined Emory University; where he currently leads the Cancer Data Science lab. His research investigates computational methods for the analysis and integration of digital pathology, genomic and clinical data with the goals of improving prognostic accuracy and disease classification.

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Notes:

Gloria Bueno, J Clin Exp Pathol 2016, 6:5(Suppl)
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AIDPATH: The 1st european project for academia and industrial collaboration for digital pathology

Gloria Bueno
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Advances in digital pathology are generating huge volumes of whole slide and tissue microarray images which are providing new insights into the causes of most devastating diseases. They also present tremendous opportunities for developing and evaluating new and more effective treatments that may revolutionize the care of patients with cancers and other diseases. The challenge is to exploit the new and emerging digital pathology technologies effectively in order to process and model all the heterogeneous tissue-derived data. This requires joint research projects and collaborative programmes between academia and industry, which will help developing efficient and innovative products to fulfil the needs of digital pathology. This is the goal of the AIDPATH project: AIDPATH is composed by 4 companies (Leica, Astrazeneca, Barco and TissueGnostics), 3 hospitals and 5 research institutions in Europe and funded by Marie Curie Actions FP7 EC-612471 during 4 years. AIDPATH facilitates the development of digital pathology by producing new products and research results tailored to fulfil their needs. The work done and the results obtained for different applications in breast and colorectal cancer as well as in nephropathology will be presented in this conference.

Biography

Gloria Bueno is a Professor and researcher at the School of Industrial EngineersUCLM in Ciudad Real, Spain since 2002.She did her PhD in Computer Vision at Coventry University in 1998. She conducted research in different centers, such as: center for Studies in Technical Research of Guipuzcoa - San Sebastian & Louis Pasteur (E), Centre National de Recherche Scientifique the Civil Hôpitaux Telecomunication School, University, Strasbourg (FR) and Gilbert Gilkes & Gordon Technology, Kendal (UK). She directs different projects of national and European research biomedical image processing. Her current interests are: signal and image processing, modeling and artificial intelligence.

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Scientific Tracks & Abstracts

(Day 2)

Christian Munzenmayer et al., J Clin Exp Pathol 2016, 6:5(Suppl)
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A web-based platform for education and quality control in cell morphology

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The morphological differentiation of cells is a challenging task for which experience and continuous qualification over many years is needed. In the field of diagnostics of variations in blood and hematopoietic organs the qualification of health personnel is of particular importance. For this reason an interactively usable knowledge and qualification platform for professionals in hematology in the area of cell morphology has been developed. The HemaWeb platform covers significant aspects of knowledge transfer, knowledge development and knowledge assurance and provides professional exchange with tutorial support and certified examinations. Fundamental information about cell morphology is contained in a case database and in a cell dictionary. Interactive test assignments provide the opportunity to check this basic knowledge. Knowledge Transfer from experts to platform users is supported by interactive discussion of clinical cases in webinars and case conferences through a discussion platform. The core element of the platform is a module for internal and external quality control (inter-laboratory tests) by means of virtual microscopy. Digitized samples are pre-annotated by a clinical expert as supervisor of the test. Participating laboratories can access and navigate slides, enter their annotations and receive automated reports on their performance. The platform has been evaluated in a several pilot studies with hematology laboratories in Germany. It provides access to high-quality slides and flexible, extra-occupational education without the obligation to be present. Improved education and training possibilities can be realized and cost-efficient execution of inter-laboratory tests with a higher grade of comparability are possible.

Biography

Christian Munzenmayer has completed his Doctorate from the University of Koblenz-Landau in 2006. Since 2000, he is with the Fraunhofer Institute for Integrated Circuits IIS, Germany. His primary research interests center on image and texture analysis, automated microscopy and digital pathology. He is the Head of the research group Medical Image Processing and Manager of the business field Digital Pathology and Laboratory Diagnostics. He is the author and co-author of over 60 publications in scientific journals and proceeding volumes and has been Reviewer for *Medical Engineering and Physics*.

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K H Ramesh, J Clin Exp Pathol 2016, 6:5(Suppl)
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An analysis of ALK polysomy detected by fluorescence in situ hybridization analysis in non-small cell lung cancer patients at montefiore medical center

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Non-small cell lung cancer (NSCLC) accounts for up to 80% of all lung cancers with an overall 5 year survival rate of about 10 to 15%. It is the leading cause of cancer-related mortality worldwide; and is responsible for 27% and 19.4% cancer deaths in the US and worldwide respectively. EGFR, KRAS, BRAF and ALK-EML4 anomalies are some of the driver mutations that have treatment and prognostic implications in NSCLC. The ALK-EML4 rearrangement has been identified in about 3 to 5% of NSCLC, with the large majority in adenocarcinoma and young patients who were light or nonsmokers. Recent studies have shown that lung cancers harboring the ALK-EML4 rearrangement are resistant to epidermal growth factor receptor tyrosine kinase inhibitors, but may be highly sensitive to ALK inhibitors, such as Crizotinib (Xalkori).

Fluorescence In Situ Hybridization (FISH) analysis using the ALK DNA probe to determine if the tumor cells have the EML4-ALK rearrangement plays a vital role in establishing a rapid cytogenetic diagnosis. It is also helpful in monitoring the progression of the disease after treatment. However, a majority (>90%) of the patients with NSCLC show polysomy (multiple copies) of the ALK gene without the rearrangement. Little is known about the behavior of tumors showing polysomy, and the disease progression in patients with such tumors. At Montefiore we have been offering FISH testing (FDA approved) for ALK rearrangement since 2011.

The aim of our study was to assess the survival difference in NSCLC patients without a history of tobacco use with ALK polysomy or the fusion oncogene. Using the Clinical Looking Glass database at Montefiore Medical Center in New York, we retrospectively identified four cases of ALK-EML4 gene rearrangement and 108 cases of ALK polysomy by FISH analysis from 2011-2014. Amongst the two groups, there were no significant differences in age (p=0.47) and there was a higher percentage of female patients in the rearrangement group than in the polysomy group (3/4 Vs.54/54). Using log-rank statistical analysis, there were no significant differences in survival from the date of NSCLC diagnosis between the polysomy and rearrangement groups (p=0.37).

In conclusion, the lack of statistical significance in survival between the two groups may suggest that the oncogenicity of polysomy of ALK and the ALK-EML4 gene rearrangement in NSCLC patients works by similar mechanisms. However, the small sample size and single center study preclude any definitive conclusions in the survival differences. With clear knowledge of mortality in the two groups with a larger cohort of patients, molecular targets can be identified or the formulation of drugs that can prolong survival. As of 2016 we have added another 65 cases to the cohort of 112 cases, and are analyzing the extended data to determine if our conclusion will differ or remain the same.

Biography

K H Ramesh a native of Bangalore, and an alumnus of Bangalore University & Kidwai Memorial Institute of Oncology, obtained his Doctoral Degree in Human Cancer Cytogenetics under the guidance of Professors M Krishna Bhargava, MD and B. N. Chowdaiah, Ph.D. He moved to the US in 1986 and completed his Clinical Cytogenetics training under the guidance of world renowned geneticist Avery Sandberg, MD at Roswell Park Cancer Institute, Buffalo, NY. At present he is the Director of Cancer CytoGenomics and Associate Professor of Pathology at Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY. He is also Adjunct Associate Professor at The University of Texas MD Anderson Cancer Center. He is a Board Certified Clinical Cytogeneticist and a Diplomate of the American Board of Medical Genetics & Genomics, and Fellow of the American College of Medical Genetics & Genomics. His expertise is in genetic testing of leukemia, lymphoma, myeloma and soft and solid tumors. His interests include global education, football, and music.

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Notes:

Elizabeth C M de Lange et al., J Clin Exp Pathol 2016, 6:5(Suppl)
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Evaluation of blood-brain barrier transport and CNS drug metabolism in diseased and control brain after intravenous L-DOPA in a unilateral rat model of Parkinson's disease

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Changes in blood-brain barrier (BBB) functionality have been implicated in Parkinson's disease. This study aimed to investigate BBB transport of L-DOPA transport in conjunction with its intra-brain conversion, in both control and diseased cerebral hemispheres in the unilateral rat rotenone model of Parkinson's disease. In Lewis rats, at 14 days after unilateral infusion of rotenone into the medial forebrain bundle, L-DOPA was administered intravenously (10, 25 or 50 mg/kg). Serial blood samples and brain striatal microdialysates were analyzed for L-DOPA and the dopamine metabolites DOPAC and HVA. *Ex vivo* brain tissue was analyzed for changes in tyrosine hydroxylase staining as a biomarker for Parkinson's disease severity. Data were analyzed by population pharmacokinetic analysis (NONMEM) to compare BBB transport of L-DOPA in conjunction with the conversion of L-DOPA into DOPAC and HVA, in control and diseased cerebral hemisphere. Plasma pharmacokinetics of L-DOPA could be described by a 3-compartmental model. In rotenone responders (71%), no difference in L-DOPA BBB transport was found between diseased and control cerebral hemisphere. However, in the diseased compared with the control side, basal microdialysate levels of DOPAC and HVA were substantially lower, whereas following L-DOPA administration their elimination rates were higher. Parkinson's disease-like pathology indicated by a huge reduction of tyrosine hydroxylase as well as by substantially reduced levels and higher elimination rates of DOPAC and HVA, does not result in changes in BBB transport of L-DOPA. Taking the results of this study and that of previous ones, it can be concluded that changes in BBB functionality are not a specific characteristic of Parkinson's disease and cannot account for the decreased benefit of L-DOPA at later stages of Parkinson's disease.

Biography

Elizabeth C M de Lange has obtained her PhD from Leiden University in 1993 and was tenured in 2004. She is the Head of the Translational Pharmacology Group at Leiden Academic Center for Drug Research (LACDR). She has published more than 100 papers and book chapters and is a Member of the Editorial Board of *FBCNS*, co-founded and co-chaired several of the international symposia on microdialysis in drug R&D. She is an AAPS Fellow since 2013.

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Eman Kandeel, J Clin Exp Pathol 2016, 6:5(Suppl)
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Estimation of stem cell frequency in acute myeloid leukemia at diagnosis: Relation to hematological and clinical parameters

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Background: Acute myeloid leukemia (AML) outcome is inferior to acute lymphoblastic leukemia. Treatment failure is largely attributed to the persistence of leukemia stem cells (LSCs) which are less accessible and hence less responsive to chemotherapeutics.

Aim: To demonstrate the impact of LSCs frequency at diagnosis and at follow up periods as compared to minimal residual disease (MRD) on overall survival (OS) and disease free survival (DFS).

Methods: The study was performed on 84 adult AML patients. Panels used CD38FITC/CD123PE/CD34ECD/CD45PE-PC5 and CD90FITC/CD133PE/CD45ECD/CD33PE-PC5 analyzed on Navios Flow cytometer. Cell populations with different surface markers were calculated using the prism function of the software. The study was performed according to Helsinki declaration for studies on human subjects and approved by the Institution Review Board (IRB) of the National Cancer Institute, Cairo University. An informed signed consent was obtained from all study subjects before enrollment.

Results: A higher CD 123% at diagnosis ($p \leq 0.001$) and at day (d) 14 ($p=0.004$ & $p \leq 0.001$ respectively) had an adverse impact on OS and DFS. A higher CD 133% at diagnosis and at d14 ($P=0.006$ & $P \leq 0.001$ and $P \leq 0.001$ & $P \leq 0.001$ respectively), had an adverse impact on OS and DFS. A higher [CD34-/CD38+/CD123+] percentage at diagnosis ($P=0.025$ and $P \leq 0.001$) had adverse impact on OS and DFS at d14 ($P=0.029$) had adverse impact only on DFS.

Conclusion: High frequency of LSCs reflects a higher percentage of chemotherapy resistant cells that will lead to the outgrowth of MRD, thereby affecting clinical outcome.

Biography

Eman Kandeel has completed her MD in 2011 from NCI, Cairo University, Egypt. She has experience of Flow Cytometry from Roswell Park Cancer Institute, Buffalo, New York. She is a Lecturer at BMT lab Clinical Pathology Department from 2011 to till date.

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Improving joint recovery of multi-channel ECG signals in compressed sensing-based telemonitoring systems through multiscale weighting

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Computational complexity and power consumption are prominent issues in wireless telemonitoring applications involving physiological signals. Compressed sensing (CS) has emerged as a promising framework to address these challenges because of its energy-efficient data reduction procedure. In this work, a CS-based approach is studied for joint compression/reconstruction of multichannel electrocardiogram (MECG) signals. Weighted mixed-norm minimization (WMNM)-based joint sparse recovery algorithm is proposed, which can successfully recover the signals from all the channels simultaneously by exploiting the inter-channel correlations. The proposed algorithm is based on a multi-scale weighting approach, which utilizes multi-scale signal information. Under this strategy, weights are designed based on the diagnostic information contents of each wavelet sub-band/scale. Such a weighting approach emphasizes wavelet sub-bands having high diagnostic importance during joint CS reconstruction. Coefficients in non-diagnostic sub-bands are deemphasized simultaneously, resulting in a sparser solution. The proposed method helps achieve superior reconstruction quality with a lower number of measurements. Reduction in the required number of measurements directly translates into higher compression efficiency, resulting in low energy consumption in CS-based remote ECG monitoring systems.

Biography

Anurag Singh is currently a PhD Research Scholar in the Department of Electronics and Electrical Engineering, IIT Guwahati, India. He has received his BTech (2009) from IET Rohilkhand University, Bareilly and MTech (Dec 2011) from Indian Institute of Information Technology, Design & Manufacturing Jabalpur in Electronics and Communication Engineering. His research interests include biomedical signal processing, multirate signal processing, compressed sensing and sparse representation.

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Mitochondrial stress in monocytes is reflected in micro-vesicles and associated with metabolic and coronary artery diseases

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Obesity's negative impact on health is well-documented. Health consequences are categorized as being the result of either increased fat mass (which leads to osteoarthritis, obstructive sleep apnea, social stigma) or an increased number of fat cells (which contributes diabetes, cancer, cardiovascular diseases). Disease processes increasing risk in association with obesity are subclinical chronic low-grade inflammation and oxidative stress which are also involved in development of cardiovascular diseases. For example, recent data suggest that increased oxidative stress in adipose tissue is an early instigator of metabolic syndrome. Given the number of symptoms and risk factors which characterize metabolic syndrome, the variability in combinations of three out of five its components, and the variability in treatments and patient responses to treatment of those symptoms, there remains a need in the art for identifying patients who are at risk for developing metabolic syndrome, T2D, and/or cardiovascular diseases. In this study we discovered RNA expression patterns related to mitochondrial dysfunction and oxidative stress in monocytes which were associated with metabolic syndrome and T2D, and identified an at-risk population for new cardiovascular events in CAD patients. For the first time, we showed that signatures in monocyte-specific micro-vesicles reflects these in monocytes and have similar predictive properties. We also found that identified gene signatures were related to obesity and atherosclerosis in mice and pigs.

Biography

Paul Holvoet is a Professor in Biomedicine at the Department of Cardiovascular Sciences at the Catholic University of Leuven. His research focuses on the interaction between oxidative stress and inflammation in the pathogenesis of metabolic and cardiovascular diseases. He is a Fellow of the European Society of Cardiology and the American Heart Association. He is first inventor on international patents related to oxidized LDL and gene signatures in monocytes and derived exosomes. He is also a Co-Founder of Tank™.

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