

DAY 1

Keynote Forum



International Conference on

Nuclear Medicine & Radiation Therapy

October 01-02, 2018 | Stockholm, Sweden

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PET IMAGING OF PROTEINOPATHIES IN NEURODEGENERATIVE DISEASE

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Biography

Stephens Andrew W has received an MD and a PhD in Biochemistry, Biophysics and Genetics from the University of Colorado. He was Board certified in Internal Medicine and had a Clinical Practice before entering Pharmaceutical Development. He is a Founder and the Chief Medical Officer at Piramal Imaging, GmbH, responsible for all clinical research and development activities including the approval of ^{18}F -florbetaben (NeuraCeq). He has more than 25 years of experience in the Pharmaceutical Industry, primarily in the areas of translational medicine, and diagnostic imaging of neurodegenerative, oncological and cardiovascular diseases. He began his pharmaceutical industry career investigating RNA Aptamers at NeXagen/NeXstar, and Gilead. As a Senior Director of Translational Medicine at OSI Pharmaceuticals, he was responsible for early clinical studies of a number of anti-cancer oral signal transduction inhibitors. Most recently, he was VP, Head of Experimental Medicine Oncology/Diagnostic Imaging for Bayer Pharma.

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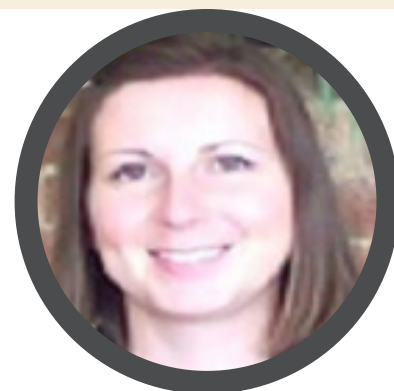
Traditional nuclear medicine ligands were designed to target cellular receptors or transporters with a binding pocket and a defined structure activity relationship. More recently, tracers have been developed to target pathological protein aggregations. Aggregations of proteins such as tau, α -synuclein, and β -amyloid ($\text{A}\beta$) have been identified in neurodegenerative diseases, including Alzheimer's disease (AD) and other dementias, and Parkinson's disease (PD). Indeed, $\text{A}\beta$ deposition is a hallmark of AD, and detection methods have evolved from coloured dyes to modern ^{18}F -labelled positron emission tomography (PET) tracers. Such tracers are becoming increasingly established in routine clinical practice for evaluation of $\text{A}\beta$ neuritic plaque density in the brains of adults who are being evaluated for AD and other causes of cognitive impairment. While similar in structure, there are key differences between the available compounds in terms of dosing/dosimetry, pharmacokinetics, and interpretation of visual reads. In the future, quantification of $\text{A}\beta$ -PET may further improve its utility. Tracers are now being developed for evaluation of tau protein, which is associated with decreased cognitive function and neurodegenerative changes in AD, and is implicated in the pathogenesis of other neurodegenerative diseases. While no compound has yet been approved for tau imaging in clinical use, it is a very active area of research. Development of tau tracers comprises in-depth characterisation of existing radiotracers, clinical validation, a better understanding of uptake patterns, test-retest/dosimetry data, and neuropathological correlations with PET. Tau imaging may allow early, more accurate diagnosis, and monitoring of disease progression, in a range of conditions. In conclusion, several PET tracers for detection of pathological protein depositions are now available for clinical use, particularly PET tracers that bind to $\text{A}\beta$ plaques. Tau-PET tracers are currently in clinical development. These tracers will continue to change our understanding of complex disease processes.

PET IMAGING OF PROTEINOPATHIES IN NEURODEGENERATIVE DISEASE

Pavlina Pike and Misty Liverett

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There has been a significant growth in the number of nuclear medicine procedures in the USA, mostly because of the significant advances in radiopharmaceuticals, instrumentation, and data analysis. Newer radiopharmaceuticals such as ^{68}Ga dota-tate (NETSPOT) can be used with PET/CT imaging to locate neuroendocrine tumors. Localizing NETs can then lead to the use of peptide receptor radionuclide therapy such as ^{177}Lu . The development of these newer radiopharmaceuticals builds upon each other to offer patients highly specific targeted imaging and molecular radiotherapy. Hybrid modalities such as SPECT/CT, PET/CT and PET/MRI are gaining popularity because of their ability to combine anatomical information from CT and MRI with functional, metabolic, or physiologic information provided by molecular imaging. The development of powerful computing algorithms has allowed scientists to extract pathophysiological information from images from different modalities, based on quantitative qualities such as texture, intensity, volume, size and shape. Radiomics is a giant step in the direction of personalized medicine as it provides means to accurately detect and diagnose tumors and assist with the choice of therapeutic strategy. Artificial Intelligence has also been employed in assisting radiologists with image interpretation by highlighting suspicious areas in the image.



Biography

Pavlina Pike has completed her PhD from the University of Tennessee in 2005. She has completed her Postdoctoral studies in Medical Physics from the University of Alabama in Birmingham in 2011. In 2013, she was certified by the American Board of Radiology in Diagnostic Imaging. She is currently employed as a Medical Physicist at the Huntsville Hospital Health System in Huntsville, Alabama.

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BIO ELECTRON'S LASER ACUPUNCTURE BY KBTE MEDICAL LASER DEVICE

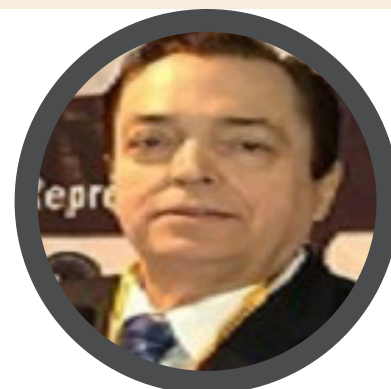
Nick Kostovic

Kostovic Acupuncture by bio Electron's Laser Corp, USA

The K-BTE device releases electrons, enriched with natural acids and is capable of melting by burning off a number of sick cells with no harm to the healthy cells. It melts by burning off and then disperses dead cells from the fiber of atrophied muscle, bone and cartilage tissue as well as plaque from the vascular system with no harm to healthy cells. The K-BTE device attracts and transfers light which consists of elemental bio electrons, photons and electron neutrinos into the brain. This fosters the regeneration, recovery and re-growth of neurons in the brain, thereby improving memory and mobility. Melting and destroying malignant cancer cells in the brain or any other physical organ accomplished with no side effects and no harm to healthy cells. Melting cleanses internal plaque from the vascular system in the brain or any other physical organ. This will prevent strokes, heart attacks, diabetes and many different neurological disorders. Melting cleanses the fiber tissue of dead cells dispersing them and making space for the formation of new and healthy cells. This is the most important step for a vital, longer lasting life. The K-BTE device has the capability to cleanse the body of radioactive radiation particles as well as different types of toxic biochemical nerve gas. This enriched electrons radiation emitting process is absolutely nonradioactive, non-toxic and is in not a shock therapy.

Definition of Bio Electrons' photons

Bio Electrons' photons are sub-elemental quanta energetic forms of bioelectricity connected in the special circuit enables us to produce RC (reverse current). RC is a carrier of a magnetic charge and unmistakably extracting, electromagnetic charges from an AC current. Electrons directly release magnetic charges in the opposite direction from its AC electrons. Loosened electromagnetic charged electrons are converted in the lower stage/grade of sub elemental quanta bio electron's photons particles. It never becomes positrons.



Biography

Nick Kostovic was graduated from Split Gymnasium in 1969 with an Associate of Arts Degree in Humanities and Science. He is an Italian and US citizen.

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Special Session



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NEW ASPECTS OF MEDICAL PHYSICS IN RADIATION ONCOLOGY AND IMAGING

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Biography

Prof. Dr. G. A. Zakaria studied physics at the University of Halle-Wittenberg in 1978, and post-graduated at the University of Goettingen and received his Ph. D in medical physics at Heidelberg University, Germany.

Prof. Zakaria is currently the chairman of the Department of Medical Radiation Physics at Gummersbach Teaching Hospital of the University of Cologne and professor of Biomedical Engineering at the University of Applied Sciences in Koethen. Furthermore he has been invited as Guest/honorary/adjunct professor in many institutes or universities in Germany, Italy, China and Bangladesh. Since January 2018, Dr. Zakaria is nominated as the Accreditation Committee-2 Chair (Radio-Oncology Physics) of the International Medical Physics Certification Board (IMPCB).

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Medical Physics is the application of physics concepts, theories and methods to medicine and health care. Medical physicists play a vital and often leading role for any medical research team. Their activities cover some key areas such as cancer, heart diseases and mental illnesses. In cancer treatment, they primarily work on issues involving imaging and radiation oncology. Thus the medical physicists play a mandatory role in every radiation oncology team. The capability of controlling the growth of any cancer with radiation dose is always associated with the unavoidable normal tissue damage. Accordingly, many physical-technical developments in radiotherapy facilities are aimed to give a maximum radiation dose to tumour cells and at the same time minimize the dose to the surrounding normal tissue. For that reason, after the development of the Cobalt 60 (^{60}Co) irradiation units in the 50 ties medical linear accelerators (linacs) were developed in the following decades. Advanced linear accelerators, helical tomotherapy and CyberKnife machines have been developed over the past two decades. Last but not least, neutrons, protons and even heavier ions have also been applied. At the same time, treatment calculation and delivery methods have been continuously improved from conventional multi-beam techniques to tumour shape conformal methods such as 3D conformal radiotherapy (3DCRT), radio surgery, intensity modulated radiotherapy (IMRT), image guided radiotherapy (IGRT), stereotactic body radiation therapy (SBRT) and adaptive radiotherapy (ART). The concentration of dose to tumour requires precise information on the shape and the anatomical geometry of the tumour within the body. The techniques providing such pieces of information in a visible form is summarized by the term of "Imaging". X-ray has played a dominant role almost from the time of its discovery in 1895. Up to now, the use of X-rays has been extended to tomographic imaging with computed tomography (CT) and other imaging modalities like ultrasound (US), magnetic resonance imaging (MRI) or positron emission tomography (PET) which have been developed over the last decades. By their combined use, the required information level on the clinical tumour target volume for radiotherapy has been tremendously raised. The physical and technical development of radiation oncology and imaging are discussed in this talk covering aspects in biology as well.

DAY 2

Keynote Forum



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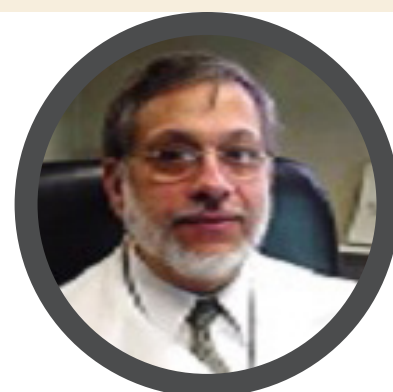
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LABELLED LEUKOCYTE/BONE MARROW IMAGING FOR DIAGNOSING INFECTION OF RECENTLY IMPLANTED LOWER EXTREMITY ARTHROPLASTIES

Christopher J Palestro¹, C Love², G G Tronco¹, K K Bhargava¹ and K J Nichols¹

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Biography

Christopher J Palestro has pioneered the use of combined labelled leukocyte/bone marrow imaging for diagnosing osteomyelitis. He has authored or co-authored more than 150 peer reviewed articles, nearly 100 book chapters and review articles. He serves on the Editorial Boards of *Radiology*, *Journal of Nuclear Medicine* and *Quarterly Journal of Nuclear Medicine and Molecular Imaging*. He is Co-chair of the Society of Nuclear Medicine and Molecular Imaging's Working Group for the Tc-99m and In-111 Labeled Leukocyte Procedure Standards/Guidelines and Chair of the Appropriate Use Criteria Committee for Inflammation and Infection. He is a Former Chair of the American Board of Nuclear Medicine. In 2013, he received the Presidential Distinguished Educator Award from the Society of Nuclear Medicine and Molecular Imaging. In 2017, he was elected as Fellow of the Society of Nuclear Medicine and Molecular Imaging, one of that organization's most prestigious awards.

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Diagnosing lower extremity prosthetic joint infection during the first year after implantation, when up to two thirds of these infections occur, is challenging. Pain usually is present, fever is variable. Leucocytosis is a poor predictor of infection. C-reactive protein remains elevated for up to three weeks. Erythrocyte sedimentation rate can remain elevated for up to one year. Joint aspiration with culture, the definitive preoperative diagnostic procedure, is specific, sensitivity is variable. Plain radiographs lack sensitivity and specificity. Data on radionuclide imaging during the early postoperative period are limited. The bone scan can exclude infection. It is a good rule out test, but cannot rule in infection. ⁶⁷Ga accumulates in normally healing surgical incisions and in aseptic inflammation. With an overall accuracy of 60%-80%, there is little role for this radiopharmaceutical in prosthetic joint infection. Data about diagnosing prosthetic joint infection with ¹⁸F-FDG in the early post-operative period are scant; uptake of this radiopharmaceutical in a variety of postoperative settings for variable time periods, however, is well known. ¹¹¹In labelled leukocytes do not accumulate in normally healing surgical wounds and combined with bone marrow imaging is about 90% accurate for diagnosing prosthetic joint infection. We reviewed combined labelled leukocyte/marrow imaging performed on 40 lower extremity arthroplasties implanted within one year before imaging, including 15 implanted within 3 months prior to imaging. Imaging results were compared to final diagnoses, which were surgically, microbiologically and histopathologically confirmed. 28/40 arthroplasties were infected including 10/15 imaged within three months after implantation. Sensitivity, specificity and accuracy were 96%, 92%, 95% respectively for all 40 arthroplasties and 100%, 80%, 93% respectively for 15 arthroplasties imaged within 3 months after implantation. Results are comparable to those reported for diagnosing prosthetic joint infection in general and indicate that during the first year after implantation, when evolving postoperative changes can confound diagnostic test results, labelled leukocyte/marrow imaging accurately diagnoses lower extremity prosthetic joint infection.

MAGNETO-PLASMONIC NANO-HETEROSTRUCTURES AS X-RAY DOSAGE BOOSTER IN RADIATION THERAPY

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Biography

Carola Kryschl has completed her PhD in Physical Chemistry from Heinrich-Heine University of Duesseldorf and Postdoctoral research studies from Stanford University. In 1993, she accomplished her habilitation thesis in Experimental Physics and became an Assistant Professor of Experimental Physics at Heinrich-Heine University of Duesseldorf. Since 2000, she is University Professor of Physical Chemistry at Friedrich-Alexander University of Erlangen. She has published 2 patents and more than 100 scientific papers in peer reviewed international journals and had been serving as a Peer Reviewer for more than 30 scientific journals in Physics, Physical Chemistry, Laser Spectroscopy, Material Sciences, Biochemistry, Biophysics, Nanotechnology, Nanomedicine, Nanotoxicology and for the Volkswagenstiftung, USA; Department of Energy and Deutsche Forschungsgemeinschaft. Her current research interests are in Nanotechnology, Nanoplasmonics, Ultrafast Laser Spectroscopy, Nanomedicine and Nanotoxicology.

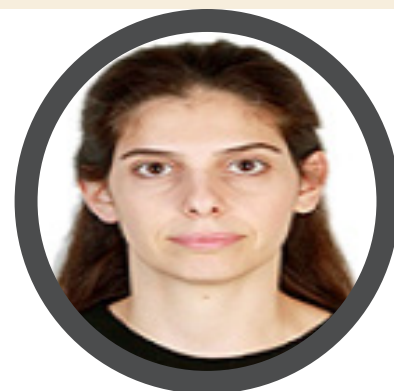
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Our primary research objective is to design magnetically targeted magneto-plasmonic nano-heterostructures (MP-NHs) that perform as multimodal nanotherapeutics for synergistic cancer therapies. Therefore superparamagnetic iron oxide nanoparticles (SPIONs) were merged with gold nanospheres, nanoclusters or nanopatches, either through a thermal decomposition procedure or via a facile co-precipitation synthesis. SPIONs with sizes around 20 nm were shown to exhibit superparamagnetism as well as to develop substantial potential as X-ray dosage enhancer when internalized by tumor cells. The Au-SPION nano-heterodimers combine high-Z material with catalytically active Fe_3O_4 surfaces and moreover, plasmonic properties with superparamagnetic performance. In case of the SPIONs, the interaction with X-rays creates through ablation highly reactive surfaces. The freely accessible Fe^{2+} and Fe^{3+} ions may efficiently catalyze in the cytoplasm with the generation of reactive oxygen species (ROS), in particular, the formation of highly reactive hydroxyl radicals (via the Fenton reaction). As boosting the ROS concentration in X-ray irradiated tumor cells for several 100%, SPIONs display a high performance as X-ray dose enhancer. For NOBF₄ stabilized Au-SPION nano-heterodimers, we could verify synergistic interactions between X-radiation and both kinds of surfaces composed either of Au atoms or Fe_3O_4 , which resulted in the simultaneous and independent formation of the nitric oxide radical at the Fe_3O_4 surface and the superoxide radical at the Au surface. The surface-confined reaction between these radicals generated peroxynitrite. This highly reactive species were observed to cause nitration of mitochondrial proteins, lipid peroxidation, and induces DNA strand breakages. As providing a synergistic nanopatform for X-ray induced formation of both, the highly reactive radical nitric oxide, superoxide and peroxynitrite, the NOBF₄ functionalized Au-SPION nano-heterodimers were shown to exhibit excellent performance as X-ray enhancing agents in radiation therapy.

TARGETING STRATEGIES OF RADIOPHARMACEUTICALS BY USING DRUG DELIVERY SYSTEMS FOR CANCER IMAGING

Derya İlem Ozdemir

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Biography

Derya İlem Ozdemir has completed her PhD from Ege University and postdoctoral studies from Stanford University School of Medicine. She is working as an Associate Professor in Ege University Faculty of Pharmacy. She has patent grants, more than 25 papers in reputed journals and has been serving as an Editorial Board Member of repute.

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Cancer is one of the leading causes of mortality worldwide. Usually, the diagnosis of cancer at an early stage is important to facilitate proper treatment and survival. Nuclear medicine has been successfully and widely used in the diagnosis, staging, therapy and monitoring of cancers by allowing scientists and physicians to see what is happening in the body at a cellular level. Radiopharmaceuticals are radioactive drugs which consist of a pharmaceutical compound and a radionuclide part. After administration, the pharmaceutical compound moves to the target tissue and the emitted radiation is detected by using gamma cameras. Since high target/non-target uptake ratio is critical in nuclear imaging studies, likewise conventional drugs radiopharmaceuticals are necessitating alternative and safer treatment drug delivery strategies. Nanomedicine has developed to resolve issues with poor drug solubility, nonspecific cytotoxicity, suboptimal pharmacokinetics and pharmacodynamics, as well as poor bioavailability. In last decades, drug delivery systems likewise include liposomes, polymeric nanoparticles, dendrimers, micelles, mesoporous silica nanoparticles and gold nanoparticles, among others are being evaluated as potential radionuclide carriers in radiopharmacy. Scientists have designed radiopharmaceuticals to accumulate both active and passive targeting. Passive targeting is a means by which drug can enter tumors due to enhanced fenestrations in tumor vasculature and take advantage of the enhanced permeability and retention (EPR) observed in solid tumor. The enhanced permeability and retention (EPR) effect allows for some selective tumor uptake and retention of nanoparticles due to the leaky tumor vasculature and poor lymphatic drainage in tumors respectively. Also by surface modifications of nanoparticles using polyethylene glycol (PEG), the circulation time of nanoparticles in the blood can extend, while the mononuclear phagocytic system (MPS) recognition and removal reducing. A multidisciplinary approach with collaborations between theoretical and experimental scientists likewise radiopharmacist, pharmaceutical technologist, medical doctors, chemist, biotechnologist etc., is therefore required to improve new targeted radiopharmaceuticals in the clinic.