

repository to support both clinical research and enhanced clinical decision support for patient management. Creation of an analytical platform to integrate, access and analyze temporal clinical data ranging from the pICU to also incorporate neo-natal ICU and pregnancy history is underway with a prototype already in testing. Analytical methods are being evaluated in collaboration with Dr. Mike Quasney (Medical College of Wisconsin) and the Virtual Pediatric ICU and PALISI (Pediatric Acute Lung Injury and Sepsis Investigators). This effort is exploring expanded international partnerships in both Europe and China to increase the accessible data for analysis and to further participate in the development of better diagnostic standards. We will present the initial state of both the analytics and platform development to encourage extension of this international effort to interested clinicians and clinical researchers. We believe that this unique approach, which focuses first on addressing the critical need to improve patient management through disease stratification will not only benefit pARDS but be extensible to many other pediatric rare disorders.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.021>

A collaborative approach to encourage research and promote new treatments for orphan diseases

Lesley Greene

Vice Chair, Committee for Orphan Medicinal Products (COMP), European Medicines Agency (EMA), London, UK

Abstract

The last two decades has seen a significant increase in the development of medicinal products to treat rare “orphan” diseases, largely due to the EU Orphan Medicinal Product Regulation (2000), but also because of the consistent advocacy by patient groups prior to this regulation. These groups from across Europe joined forces under the umbrella of EURORDIS, to secure the implementation of the regulation and ensure that there was patient representation on the committee at EMA (the European Medicines Agency) which would be responsible for assessing and giving opinions on applications, namely COMP (The Committee for Orphan Medicinal Products). As its Vice-Chair I have the privilege to ensure the patient perspective is always considered during these assessments. I will discuss how COMP works as part of the EMA Human Medicines Research and Development Support Division to promote the development of research into medicinal products for the treatment of rare diseases and how this is also encouraged by EU funding through Horizon 2020. Since rare diseases are a global issue, I describe how the EU is also collaborating with IRDiRC (the International Rare Disease Research Consortium) to provide the critical mass in terms of patient population and skills needed to meet the urgent need for new therapies as quickly as possible.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.022>

Disease systems modeling for discovery of mechanistic biomarkers

Erfan Younesi

Fraunhofer Institute for Algorithms and Scientific Computing SCAL, Sankt Augustin, Germany

Abstract

The use of biomarkers is becoming increasingly integral to the contemporary practice of medicine and continues to play a central role in preventive, predictive and personalized medicine. However, the limited number of FDA-approved, in use biomarkers, on one hand, and an increasing number of published potential biomarkers, on the other hand,

calls for an accelerated approach to translating biomarker research to clinical application. In this talk, I introduce novel concept of “Biomarker-guided Mechanism Discovery” through an integrative disease modeling approach and present the successful application of this methodology to deciphering the network model of genomic hormone interactions underlying dementia and its translational validation through serendipitous off-target effect. Moreover, the current challenges in biomarker discovery is discussed and results of our proposed Biomarker Ontology in collaboration with pharma industry will be presented.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.023>

Three-dimensional normal human neural progenitor tissue-like assemblies: A model for persistent Varicella-zoster virus infection and platform to study oxidate stress and damage in multiple hit scenarios

Thomas J. Goodwin^a, M. McCarthy^d, N. Osterrieder^b, R.J. Cohrs^c, B.B. Kaufert^b

^a Disease Modeling/Tissue Analogues Laboratory, NASA Johnson Space Center, Houston, Texas

^b Institut für Virologie, Freie Universität Berlin, Berlin, Germany

^c Department of Neurology, University of Colorado School of Medicine, Aurora, Colorado

^d University of Texas Medical Branch at Galveston, Galveston, Texas

Abstract

The environment of space results in a multitude of challenges to the human physiology that present barriers to extended habitation and exploration. Over 40 years of investigation to define countermeasures to address space flight adaptation has left gaps in our knowledge regarding mitigation strategies partly due to the lack of investigative tools, monitoring strategies, and real time diagnostics to understand the central causative agent (s) responsible for physiologic adaptation and maintaining homeostasis. Spaceflight-adaptation syndrome is the combination of space environmental conditions and the synergistic reaction of the human physiology. Our work addresses the role of oxidative stress and damage (OSaD) as a negative and contributing Risk Factor (RF) in the following areas of combined spaceflight related dysregulation: i) radiation induced cellular damage [1,2] ii) immune impacts and the inflammatory response [3,4] and iii) varicella zoster virus (VZV) reactivation [5]. Varicella-zoster (VZV)/Chicken Pox virus is a neurotropic human alphaherpesvirus resulting in varicella upon primary infection, suppressed by the immune system becomes latent in ganglionic neurons, and reactivates under stress events to re-express in zoster and possibly shingles. Our laboratory has developed a complex three-dimensional (3D) normal human neural tissue model that emulates several characteristics of the human trigeminal ganglia (TG) and allows the study of combinatorial experimentation which addresses, simultaneously, OSaD associated with Spaceflight adaptation and habitation [6].

References

- [1] Cucinotta FA, Manuel FK, Jones J, Iszard G, Murrey J, et al. (2001) Space radiation and cataracts in astronauts. *Radiat Res* 156: 460-466
- [2] Blakely, EA (2000). Biological effects of cosmic radiation: Deterministic and stochastic. *Health Physics* 79:495-506
- [3] Crucian BE, Stowe RP, Mehta S, Uchakin P et al., (2013) Immune System Dysregulation Occurs During Short Duration Spaceflight On Board the Space Shuttle. *J. Clin. Immunol*, 2013, Volume 33, 456-465
- [4] Crucian BE, Stowe RP, Pierson DL, Sams CF, (2008) “Immune system dysregulation following short- vs long-duration spaceflight”, *Aviat Space Environ Med. Sep*;79(9):835-43
- [5] Cohrs RJ, and Gilden DH (2007) Prevalence and abundance of latently transcribed varicella-zoster virus genes in human ganglia. *J Virol* 81: 2950-2956

[6] Goodwin TJ, McCarthy M, Osterrieder N, Cohrs RJ, et al., (2013) "Three-Dimensional Normal Human Neural Progenitor Tissue-Like Assemblies: A Model of Persistent Varicella-Zoster Virus Infection". *PLoS Pathog* 9(8): e1003512. 10.1371/journal.ppat.1003512.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.024>

Satellite symposium: Emerging role of microwave imaging technology (organized by the biomedicine and molecular biosciences COST action TD1301) Microwave Imaging for Breast Cancer Detection

Martin O'Halloran

National University of Ireland, Galway, Ireland

Abstract

Breast cancer is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed in 2012. This represents about 12% of all new cancer cases and 25% of all cancers in women. The current standard method for detecting non-palpable early stage breast cancer is X-ray mammography. Despite the fact that X-rays provide high-resolution images at low radiation doses, its limitations are well documented. In the U.S., up to 75% of all malignancies identified by X-ray mammography are later found to be benign after biopsies. These false positive conclusions result in unnecessary biopsies, causing considerable distress to the patient and an unnecessary financial burden on the health service. Much more worryingly, up to 15% of all breast cancers present at the time of screening are missed by conventional mammography, often delaying treatment to the point where it's no longer effective. One of the most promising alternative imaging modalities is Microwave Imaging. Microwave Imaging is based on the dielectric contrast between healthy and cancerous breast tissue at microwave frequencies. Microwave imaging is non-ionising, non-invasive, does not require uncomfortable breast compression, and is potentially low cost.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.025>

Microwaves for medical imaging: Some possible pathways for an accelerated progress towards clinical practice

Lorenzo Crocco

National Research Council, Napoli, Italy

Abstract

The talk will start from a brief review of the physical basis of microwave imaging for medical diagnostics and of the challenges that have to be faced in this technology, to present three areas which are possibly the most promising ones for a fruitful application of microwave imaging in the medical arena. The first one is the monitoring of brain injuries, which is a topic of increasing importance for its impact on the European health system in the ageing society. In particular, it will be discussed how microwave imaging can play a role both in the detection of the diseases in the early stage and in their clinical follow-up, by filling the gap between current diagnostic modalities and the need of continuous monitoring at the patient's bed. The second one is the potential of enhancing the capabilities of microwave imaging by means of contrast agents. Indeed, while contrast enhancement is a common practice to improve performances in medical imaging, it presents even some remarkable and specific advantages in microwave imaging, provided suitable contrast agents are adopted. Third, and not last, the intrinsically dual nature of microwaves, which are not only a diagnostic tool, but also a therapeutic

means (hyperthermia, thermo-ablation), makes them a suitable candidate to address the emerging paradigm of theranostics, wherein the imaging capability provide the basis for truly patient specific treatments.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.026>

Hyperthermia applications at microwave frequencies

Jan Vrba

Czech Technical University Prague, Prague, Czech Republic

Abstract

Short introduction to microwave hyperthermia from the point of view of biology and physics will be given firstly. The physical basis of microwave thermotherapy for cancer treatment and for other medical microwave therapeutic purposes (e.g. in cardiology, urology, surgery, physiotherapy, etc.) will be described in this talk. Different kinds of hyperthermia clinical applications will be mentioned (i.e. local, deep local, regional and intracavitary treatment). Different physical and technological approach to describe these above given different cases will be discussed. For each of these mentioned cases a different type of electromagnetic (EM) wave should be used: EM plane wave for local treatment, converging cylindrical EM wave for regional treatment and finally diverging cylindrical EM wave for intracavitary treatment. Then different types of applicators (resp. antennas) for microwave hyperthermia clinical applications will be discussed (e.g. waveguide, waveguide horn, evanescent mode, planar, array, lens, metamaterial etc. applicators). Each of these microwave technologies has its specific advantages in creation of the optimal SAR and temperature distribution in the area to be treated. It is given by its specific EM field distribution in the aperture of these applicators. And the importance of the so called treatment planning will be discussed. It is based on several different numerical methods (e.g. FDTD, FEM, MOM etc.) for calculation of the SAR in the treated area firstly and afterwards for calculation of the temperature distribution in the treated area with respect to the time, blood perfusion, etc. Last part of this presentation will be dedicated to description of clinical results of hyperthermia in cancer treatment. Importance of possibility to combine effectively hyperthermia with e.g. radiotherapy and/or chemotherapy will be underlined.

<http://dx.doi.org/10.1016/j.nhtm.2014.11.027>

Other applications of medical microwaves – Breast tumour classification

Raquel Conceição

University of Lisbon, Lisbon, Portugal

Abstract

This talk addresses the development of imaging techniques for the early detection of breast cancer, based on Ultra Wideband (UWB) radar, a promising emerging technology that exploits the dielectric contrast between normal and tumour tissues at microwave frequencies. Of particular interest in this work are issues related to techniques for classification of potential breast tumours into benign and malignant. This is particularly important given the results from recent studies of the dielectric properties of breast and tumour tissue, which have found that strong similarities exist between the dielectric properties of malignant, benign and normal fibroglandular breast tissue. This creates a more challenging imaging scenario and motivates the development of enhanced signal processing techniques for UWB imaging systems.

Tumour growth and development patterns are modelled using Gaussian Random Spheres, using four discrete sizes and four different shapes.