[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.

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

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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.

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

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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.

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Hyperthermia applications at microwave frequencies

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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.

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Other applications of medical microwaves – Breast tumour classification

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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.

Feature extraction methods including Principal Component Analysis (PCA), Independent Component Analysis (ICA) and Discrete Wavelet Transform (DWT), are used to extract the most relevant features from the detailed Radar Target Signatures of the tumours, which are then classified with a number of different classification techniques: Linear Discriminant Analysis (LDA), Quadratic Discriminant Analysis (QDA) and Support Vector Machines (SVM). In addition to these techniques, a number of different multi-stage classification architectures are considered. The feature extraction and classification algorithms are evaluated for both homogeneous and heterogeneous breast tissue models, for a range of different tumour sizes and shapes.

Also, the first experimental results using a pre-clinical UWB prototype imaging system for tumour classification based on the shape of tumours. A database of benign and malignant tumour phantoms was created using dielectrically–representative tissue-mimicking material. Classification of benign and malignant tumour models of the experimental data was completed with Linear Discriminant Analysis, Quadratic Discriminant Analysis and Support Vector Machines classifiers.

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Preventive handling of drug nephrotoxicity with antioxidant cotherapies: Preclinical studies and clinical perspectives

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Abstract

Worldwide, nephrotoxicity poses a considerable health and economic burden. Nearly 25% of the top 100, most used drugs in intensive care units are potentially nephrotoxic. Moreover, nephrotoxicity causes 10-20% of the acute renal failure cases (ARF). ARF is a very serious condition with high incidence and mortality rate, which is estimated at approximately 50% of the cases despite dialysis application, especially within critically ill patients. Mortality increases to 80% when ARF courses with multi-organ damage. The clinical handling of renal injury and ARF is difficult and expensive because, other than dialysis, there are no available treatments. For this reason the search for strategies to prevent nephrotoxicity constitute an active area of investigation. In addition to drug targeting and medical chemistry for new and safer molecules, a line of interest is the identification of renoprotective adjuvants for co-administration along with potentially nephrotoxic drugs.

At the preclinical level, many chemically unrelated antioxidants have been shown to protect the kidneys from cisplatin nephrotoxicity, especially in experimental animal models. They include curcumin, N-acetylcysteine, naringenin, selenium, vitamin C, vitamin E and other dietary components that scavenge free radicals formed by exposure to cisplatin. Although promising, antioxidants have not yet demonstrated a clear benefit in the clinical research conducted so far, which requires further investigation. In this line, a pre-clinical selection of candidates to be assayed at the clinical level must be pursued in order to (i) improve the efficacy of the preclinical-to-clinical transition; and (ii) to reduce early failure rate in clinical assays through the drug discovery process.

One of the main problems identified in the translation of antioxidants to the clinical practice is their very low bioavailability derived from a very low absorption upon oral administration. Our research line has been focused on the effect of the natural antioxidants resveratrol and quercetin, and the antidiabetic metformin, at preventing drug nephroxicity. Our studies clearly show their renoprotective effect at the preclinical level. We are testing these molecules in the clinical setting and developing new nanoformulations which will enhance their solubility and, hence, their bioavailability to prospectively achieve clinical utility.

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Restoring the function of the glutamate-nitric oxide –cGMP pathway by treatments acting on different brain targets restores cognitive function in rats with minimal hepatic encephalopathy

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Abstract

Chronic liver disease (e.g. cirrhosis) affects brain function. There is a high incidence of mild cognitive impairment and psychomotor slowing in patients with cirrhosis. This condition, known as minimal hepatic encephalopathy (MHE) affects more than 2 million people in the European Union and has serious health, social and economic consequences. There are no effective treatments for MHE.

Rat models of MHE reproduce cognitive and motor alterations seen in patients, showing reduced performance in different types of cognitive tests, including learning a conditional discrimination task in a Y maze. We have shown that reduced ability to learn the Y maze task is due to reduced function of the glutamate-nitric oxide (NO)-cGMP pathway in cerebellum, assessed in vivo by microdialysis. This results in reduced formation of cGMP in response to activation of NMDA receptors and impairment of learning ability. We have found that both hyperammonemia and neuroinflammation contribute to impair this pathway. The effect is mediated by enhanced tonic activation of NMDA and GABAA receptors and of MAP-kinase p38. Based on this mechanistic studies, we have designed and tested new therapeutic strategies acting on specific targets in the brain, which have successfully restored the function of the glutamate-NO-cGMP pathway in vivo and learning ability in rats with MHE. This can be achieved by therapeutic treatments using:

a) phosphodiesterase 5 inhibitors (sildenafil, zaprinast), that increase cGMP levels by reducing its degradation
b) extracellular cGMP
c) antagonists of type A GABA receptors (bicuculline)
d) neurosteroids that modulate GABAergic tone (pregnenolone sulfate)
e) inhibitors of cyclooxygenase (ibuprofen) which reduce neuroinflammation
f) inhibitors of MAP- kinase p38 (SB239063), that reduce microglial activation and neuroinflammation
g) Translation of some of these treatments to clinical practice would improve cognitive function, quality of life and life span of patients with cirrhosis and MHE and reduce health systems costs.

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Modeling and simulation the conduit connecting translational medicine with portfolio management

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Abstract

Translational medicine science and the volume of information generated in this field have grown exponentially in the last decade and continue to grow faster every day. This has generated a huge amount of data. The application of