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Foreword: The Clinical Application of Magnetic Resonance Imaging and Spectroscopy Techniques in the Characterization of Tumor Processes

Lester Kwock, Ph.D.

University of North Carolina
School of Medicine
Department of Radiology
CB# 7515
Chapel Hill, North Carolina
27599-7515 USA

www.tcrt.org

Nuclear magnetic resonance imaging, which is commonly referred to as magnetic resonance imaging (MRI) in medicine, is a powerful technique that has been shown to give exquisite anatomical information concerning tumor location and extent of tumor involvement in tissues. Part of the development of MRI was due to Dr. Raymond Damadian who in 1971 showed that magnetic resonance might be useful in detecting cancer in humans. This was based on his observations that cancerous processes in tissues exhibits longer water proton relaxation times and was an impetus for the development of *in vivo* MRI (1, 2). However, it was Dr. Paul Lauterbur and Dr. Peter Mansfield who developed the MRI technology and concepts that are used today in routine clinical practice to obtain cross-sectional images of not only cancerous processes in tissues but other disease processes (3, 4).

Magnetic resonance is not a single technique that just generates anatomical images but is a multiple modality technique that can also non-invasively generate metabolic and physiological information regarding tumor processes. It is a technology which has been awarded two Nobel Prizes. The first Nobel Prize was awarded to Drs. Felix Bloch and Edward Purcell in 1946 for their pioneering work on nuclear magnetic resonance spectroscopy (MRS). Their work opened up a whole new field in analytical, organic, and biochemistry which today has opened up probably one of the most powerful non-invasive methods to study the metabolism of cancerous processes and to monitor the effects of treatment on these processes both *in vivo* and *in vitro*. In November of 2004, a workshop sponsored by the National Cancer Institute of leading MR spectroscopists and imagers from the United States and Europe will be held in Bethesda, Maryland to develop a consensus report on the clinical application of MRS and dynamic contrast MRI in monitoring tumor responses to treatment.

The second Nobel Prize in magnetic resonance was awarded to Drs. Paul Lauterbur and Peter Mansfield in 2003 for their work in the development of magnetic resonance imaging. This work has not only lead to the development of the routine cross-sectional anatomical imaging of the human body but has lead to the development of perfusion and diffusion MRI techniques to examine physiological processes such as tumor angiogenesis and proliferative/destructive tumor processes.

In this issue of *Technology in Cancer Research and Treatment* are presented papers from a group of dynamic investigators who have utilized MRI and MRS techniques to develop new methodologies and strategies to classify and detect

Corresponding Author:
Lester Kwock, Ph.D.
E-mail: kwock@med.unc.edu

tumor processes *in vivo* and *in vitro* from biopsy tissue. The methodologies discussed in these papers are generic and can be applied to the investigations of other tumor systems.

The first set of papers deals with breast cancer. Dr. Pavic, *et al*. reviews the role MRI has played in the diagnosis and management of breast cancer and the role in can play in monitoring high-risk patients. In the second paper, utilizing MRI parameters, proton MRS, and sodium-23 MRI, Dr. Jacobs group describes a multiparametric and multinuclear MRI and MRS process to obtain an *in vivo* tissue signature of breast cancer non-invasively. In contrast, Dr. Lean's paper describes a Statistical Classification Method of proton MRS data obtained from fine needle aspirates of breast tissue that can be used to determine the grade and receptor status of primary breast lesions.

In the case of the brain tumors papers, Dr. Law's paper has utilized both *in vivo* MRI and MRS techniques to better differentiate brain tumors from other pathological processes which mimic tumor processes. This has been a major problem when examining single solitary gadolinium-enhancing lesions in the brain which show similar proton MRS spectral patterns. However, by using spectroscopic imaging techniques to examine volumes not only in the enhancing area but also peri-lesional volumes and dynamic contrast enhanced MRI, has lead to a more specific differentiation of tumor from non-tumor processes. Dr. Ulmer's paper is a paper which uses both functional MRI (fMRI) and diffusion tensor MRI (DTI) to map out "the proximity of tumor borders to eloquent brain systems sub-serving language speech, vision, motor, and pre-motor functions". The preliminary data presented in this paper indicates that preoperative planning utilizing these two techniques may decrease dramatically the morbidity normally associated with brain tumor resection in patients. The papers by Drs. Bullitt and Prakh, have utilized the 3D "time of flight" MR angiography technique to obtain quantitative information regarding tumor vessel tortuosity. Their preliminary studies show that vessel tortuosity can be used to assess the response of high grade brain tumors to various therapeutic regimens and to detect tumor recurrence.

In the last paper, which deals with prostate cancer, Dr. Cheng has applied proton high-resolution magical angle spinning MR spectroscopy (HRMAS) for examining biopsy samples of prostate cancer. This is a potentially important technique which can lead to the discovery of new biomarkers of cancerous processes. The importance of this technique is that it is non-destructive. Core biopsy samples obtained can first be analyzed for MR metabolic spectral patterns and then subsequently undergo histological, immunohistochemical, and genetic analyses. This methodology can link the pathological, biochemical, and metabolic assessment of tumors to identify increases or decreases in processes related to the malignant characteristic of the tumor. Dr. Cheng's paper deals with the first link in applying this technology and that is the correlation of MR spectral data obtained using HRMAS to the assessment of the histological findings using a newly developed technique to quantitate changes in pathology.

The advances in MRI and MRS presented in this issue of *Technology in Cancer Research and Treatment* bodes well for the future of this technology in assessing tumor processes both *in vivo* and *in vitro*. The development of new methodologies and information obtained in studies on tumor processes that are being examined on cells and animal models utilizing high field systems (>4 T) will eventually be developed and performed on cancer patients since higher field whole body MR scanners have been developed. Because of signal-to-noise problems at the clinically relevant magnetic field of 1.5 T, only nuclei such as protons and phosphorous MR techniques have been used to monitor cancer patients routinely. With the increase in magnetic field strengths, enriched carbon-13 labeled metabolites and other important nuclei can be used to monitor tumor processes with MRI or MRS to detect changes in metabolic pathways or receptors that can be used to: (i) detect and determine the malignant character of the tumor, (ii) to develop new treatment paradigms depending on the malignant character of the tumor, and (iii) monitor the response of the new treatment paradigm. The development of newer acquisition techniques such as integrated parallel acquisition (iPAT) will allow studies utilizing these labeled nuclei to be performed in an acceptable time in patients.

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