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Noninvasive risk stratification of patients using predictive biomarker apoptosis index of tumors

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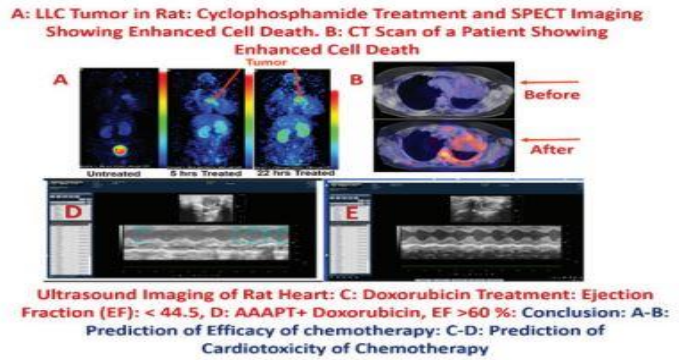
Abstract

Statement of the Problem: Human tumors are heterogeneous which evoke different responses from different treatments. Current animal models used in cancer research are xenografts which would not mimic human tumors. A noninvasive imaging modality to assess cell death in target and non-target organs simultaneously may help to overcome the heterogeneity and may identify a biomarker which can be used to predict the efficacy and toxicity of treatments. Apoptosis Index (AI) is the measure of cell death in tumor, the modulation of which reflects how it responds to therapy. For example, we and others have shown that lower the spontaneous AI, lower the response and vice versa from the treatments irrespective of the nature of treatments. We have developed a novel technology "A Priori Activation of Apoptosis Pathways of Tumor" (AAAPT) which raises AI of spontaneous tumors above a threshold level in order to evoke a better response from therapy.

Methodology & Theoretical Orientation: Cancer cells have ability to enhance survival pathways (e.g. NF-kB and PARP) and down regulate the cell death pathways (e.g. CD95, ASK1) for their survival. Hence, we have designed new technology to target these pathways to sensitize those resistant tumor cells using targeted activation technology. We have used clinically oriented SPECT and Ultrasound Imaging techniques to assess AI as a predictive biomarker of efficacy and toxicity of chemotherapy respectively.

Findings: SPECT imaging of Lewis Lung Carcinoma (LLC) showed an enhanced cell death (higher AI) post treatment by Cyclophosphamide while, US imaging reversed the cardiotoxicity by doxorubicin by using AAAPT as a neoadjuvant to Doxorubicin.

Conclusion & Significance: The noninvasive assessment of AI (measure of cell death) by SPECT combined with US imaging can be used to risk stratify patients in terms of who responds to which therapy earlier compared to tumor regression timelines.



A: LLC Tumor in Rat: Cyclophosphamide Treatment and SPECT Imaging Showing Enhanced Cell Death. B: CT Scan of a Patient Showing Enhanced Cell Death

Ultrasound Imaging of Rat Heart: C: Doxorubicin Treatment: Ejection Fraction (EF): < 44.5, D: AAAPT+ Doxorubicin, EF >60 %: Conclusion: A-B: Prediction of Efficacy of chemotherapy: C-D: Prediction of Cardiotoxicity of Chemotherapy

Speaker Biography:

Raghu Pandurangi started his scientific career Ph.D in spectroscopy followed by post-doctoral training at Radiology and Internal medicine, University of Missouri, Columbia where he remained as a faculty for 10 years. He was a principle investigator position in Shering AG, Germany where he directed and involved in 2 FDA approved drugs (AccuTect and NeoTect). He was a team leader at Mallinckrodt directing apoptosis imaging. He became an entrepreneur in 2013 inventing AAAPT technology for improving FDA approved drugs. Currently, he is the Founder, President and CSO of Sci-Engi-Medco Solutions (SEMCO) and Amplexi-LLC, recipient of several NIH grants and awards.

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