FINAL REPORT

Project Title: A Quantitative Imaging-based Biomarker for Assessment of Therapy Response in Soft Tissue Sarcomas by Differential Volume Estimation Of Viable and Non-viable Tumor Fractions

Project Number: SFA10-29

1. Date project was initiated: June 1st 2010.

2. Period covered by this report: From June 1st 2010 To 31st May 2011.

3. Publications, Abstracts, and Presentations:

   a. List all manuscripts submitted for publication during the period covered by this report resulting from this project. Include those in the categories of lay press, peer-reviewed scientific journals, invited articles, and abstracts. Each entry must include the author(s), article title, journal [book, editors(s), publisher, volume number, page number(s), and date.]

(1) Lay Press: ---

(2) Book Chapters:

a). **Singh AK,** Harris GJ, Cai W, Yoshida H. Principles of 3D post-processing, 'Image techniques-post processing' Abdominal Imaging, Elseviers, November-2010, Volume I; Section 6; Chapter: 24. Pg-154-172. (Principles of study image post processing techniques discussed).

b). **Singh AK,** Harris GJ, Cai W, Sahani DV. Advanced applications of post-processing, 'Image techniques-post processing' Abdominal Imaging, Elseviers, November-2010, Volume I; Section -6; Chapter: 25. Pg-174-198. (Computer-aided detection technique for tumor components discussed).

(3) Peer-Reviewed Scientific Journals:--

(4) Invited Articles:

a). Radiological Society of North America (RSNA) 2010- **Exhibit-Invitation for publication from Radiographics** for publication of scientific findings of liver and soft tissue sarcoma viable tumor tissue estimate study-April 2011. Quantification in Imaging Reimagined:

Evidence-based Approach in Exploring Imaging Biomarkers. Abstract ID: (9009178)-(Under preparation). *(Invited submission for RSNA 2010 Research Trainee Prize).*

b). RSNA 2010 presentation: Emerging 3D post processing techniques in Imaging of soft tissue sarcoma's: Considerations with Evidence-Based Overview. July 2011. American Journal of Roentgenology. Section Editor: Dr M. Kalra. (Submission Deadline: August 31st 2011-under preparation).

c). RSNA 2010 presentation: Fractional 3D Tumor Quantification Techniques in Assessment of Treatment Response in Oncology. July 2011. American Journal of Roentgenology. Section Editor: Dr M. Kalra. (Submission Deadline: August 31st 2011-under preparation).

d). RSNA 2010 presentation: Scientific Presentation CODE: SSA13-04 titled "MR Imaging-based Necrosis Quantification in Treated Soft Tissue Sarcoma with Existing Quantification Methods: Comparison with Partial Tissue-stained Pathological Scores'-Invited for original article 'Journal of Clinical Imaging Science'. *(Invited submission for RSNA 2010 Research Trainee Prize).*

e). RSNA 2010 presentation: Scientific Presentation CODE: SSA13-04 titled "MR Imaging-based Necrosis Quantification in Treated Soft Tissue Sarcoma with Existing Quantification Methods: Comparison with Partial Tissue-stained Pathological Scores"- -Invited for original article 'Journal of Clinical Imaging Science'.

AWARD: RSNA Exhibit – **CUM LAUDE Award. A K Singh,** MD, H Yoshida, PhD; D I Rosenthal, MD; G J Harris, PhD. The Emergence of Volumetry as an Imaging Biomarker: An Evidence-based Overview. Abstract ID: 8009483.

b. List presentations made during the last year (international, national, local societies, etc.). Use an asterisk (*) if presentation produced a manuscript.

1). Radiological Society of North America (RSNA) 2010- **A K Singh,** MD, G J Harris, PhD. Novel Quantitative Imaging Approach for Diagnostic Oncology Policy Research: Preliminary Data Structure Based on Fractional Tissue Quantification in Visceral and Soft Tissue Tumors. ID: SGI 9013025. (Manuscript under preparation).

2). Radiological Society of North America (RSNA) 2010- **A K Singh**, MD; D C Harmon, MD, MD, G J Harris. MR Imaging-based Necrosis Quantification in Treated Soft Tissue Sarcoma with Existing Quantification Methods: Comparison with Partial Tissue-stained Pathological Scores. ID: SMK 9011961. (Manuscript under preparation).

3). Radiological Society of North America (RSNA) 2010- **A K Singh**, MD; D.V. Sahani, MD, D C Harmon, MD, G J Harris PhD, J.H. Thrall, MD. Quantification in Imaging Reimagined: Evidence-based Approach in Exploring Imaging Biomarkers. ID: 9008787. (Invitation for Publication from Radiographics Journal). Abstract ID: (9009178)

4). American Roentgen Ray Society (ARRS) 2010: Kurra V. **Singh AK,** Harmon D, Chen Y, Cai W, Choy E, McGowan J, Harris GJ. Feasibility analysis with existing quantification methods for MRI-based necrosis volume estimation in treated soft tissue sarcomas: Analysis based on tumor size, grade & tissue characteristics. Abstract # 2166.

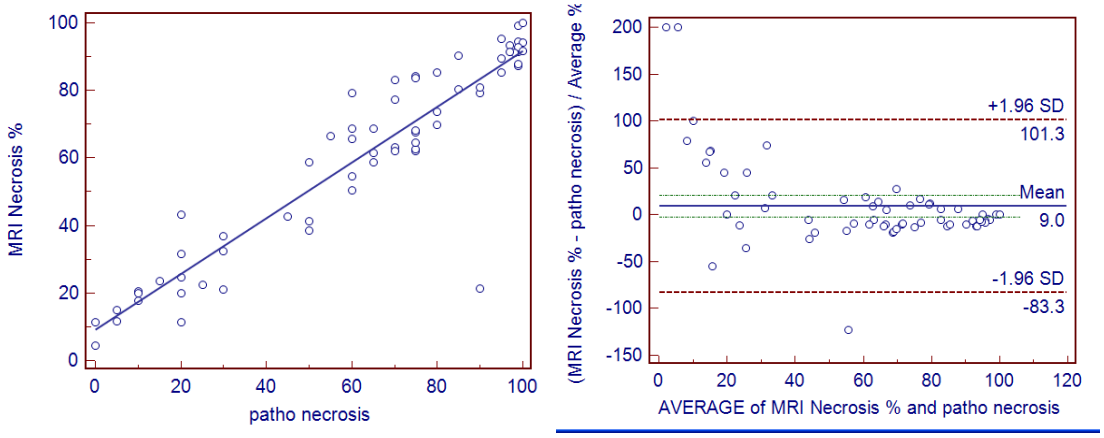
(In addition to above, 2 presentations & 1 exhibit based on study findings have been accepted for RSNA 2011 conference to be held in Chicago-November 2011).

4. Provide a brief list of keywords: (limit to 20 words)

   Soft tissue sarcoma, computer-aided detection, Magnetic Resonance Imaging (MRI), Quantification, viability, pathology, necrosis, 3D Imaging, liposarcoma, myxoliposarcoma, rhabdomyosarcoma, fibrosarcoma, malignant peripheral nerve sheath tumor, resection margin, RECIST, treatment-planning, perfusion, dynamic MRI, clinical trial.

5. Summarize the progress during the period of this report and its impact on your plans for the remainder of the project. Include a summary of the progress toward the Achievements of the originally stated aim and list the significant results:

We are pleased to report that we have made significant progress on this project. The objective was to retrospectively quantify the tumor contrast-enhancing portions in soft tissue sarcoma's that were resected using the one week prior-resection pre-surgical MRI datasets. We found a good correlation between the viability and necrosis percentage that were reported by the pathologist and the total estimates of the same variables that were estimated by using computer-aided post processing techniques in our 3D laboratory ($r=0.855$; $p<0.0001$) on the MRI datasets. The Bland-Altman analysis revealed less than 5% outliers from the standard deviation. The study findings have encouraged designing a prospective study for which we have a 10 patient data now and are comparing the histopathology slice –by-slice estimates that are taken immediately after the surgery and are matching the cell type and their locations on pathology slide to the corresponding MRI slices. We are in process of preparing a multi-year grant proposal with involvement of medical oncology, pathology and surgical oncology where we will be performing comparisons on prospective basis and categorize results, based of presurgical treatment that will be used in such tumors.



*Reports due by 31 July 2011

6. In layperson's terms, summarize the progress during the period of this report.

We are pleased that we have made good progress on this project. The idea was to estimate volumes of viable and dead tumor tissue left after treating the muscle tumors by post processing one-week prior MRI scans of patients through computer aided techniques on 3D workstations and compare it with estimates reported by pathologist who actually see the tumor cells after they are resected and report their estimates. This will provide a more effective measure to estimate response to cancer medicines in such patients. We found that viable and dead tumor tissue in such tumors after excision that was reported by the pathologist and the estimates obtained by proposed computer-aided technique using MRI datasets were similar. This has led us to design a prospective study with an extended multi-year timeline where we will involve physicians who treat such patients by drugs, and surgeons who operate on such patients along with the pathologist who report the viable & dead tumor tissue scores after tumor excision.

Explain any medical significance or implications of your results to date:

The study objective has been unanimously encouraged by our sarcoma clinical group and findings have been felicitated on eminent conference platforms in form of encouraging moderator comments, invitations from various journals and awards. The success in validating the study hypothesis will propel standards of estimating treatment-response to drugs and radiotherapy in bone and soft tissue sarcoma's.

(ANAND K. SINGH, MD) 08/11/2011.

Principal Investigator (signature) Date

_____ 08/15/2011.

Department Chair (signature) Date