Results: In 2013, a total of 1033 CT examinations were performed in 763 children (424 boys and 339 girls). Of the 1033 examinations, the main target site was the brain/head and neck in 31.6%, followed by the thorax (17.6%), abdomen (16.9%), and bone/soft tissue (13.6%). Traumatic injuries were the reason for undergoing CT in 9.8% (101 of 1033 examinations; 95% confidence interval, 8.0-11.6%). Among the 763 children, 66.1% underwent repeat CT after the first examination, and 19.3% underwent CT eight times or more. Among all examined children, 8.8% had cancer and 4.7% had cancer-prone conditions such as Down syndrome, tuberous sclerosis, and cirrhosis. Only 11.4% of the 763 children underwent CT because of trauma. The rate of trauma decreased with an increase in the frequency of CT examinations. As many as 32.2% of the children had some types of congenital anomaly.

Conclusion: Since the incidence of congenital anomalies is below 2.5% in the general population, it was concluded that the population of children undergoing CT is completely different from that not undergoing CT. It was reported that children with birth defects had a higher risk of cancer compared with children without birth defects, with a relative risk estimated to be approximately 3.0. The two groups should not be compared.


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Liquid Biopsy using “Cell—Free DNA” as Predictive Marker of Response after Radiotherapy in Solid Tumors

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Purpose/Objective(s): The use of “Liquid biopsy” using circulating cell-free DNA (cfDNA) is gaining importance as predictive marker for monitoring treatment outcome in cancer patients. We investigated the clinical significance of cfDNA monitoring in patients with solid tumors treated with radiotherapy (RT).

Materials/Methods: Twenty patients aged 37-74 yrs (median age 55.5yrs) diagnosed with advanced/metastatic cancers, on RT were recruited in an IRB-approved prospective study. Blood samples were collected before starting RT (T1), during RT (T2) and 30 and 60 days after RT (T3 and T4 respectively). The cohort comprised of 6 Lung, 4 stomach, 4 cervical and 6 Breast cancer patients. The cfDNA was purified using a QIAamp CircuPrep kit, and high-DNA (HDNA) groups. The pre-RT HDNA in the cohort was quantified and the quality was established using an ALU-based qPCR assay on an AriaMax Real-time PCR System (Agilent, USA).

Results: The cfDNA levels ranged from 1.2-14 ng/mL pre-RT and 2.5-68 ng/mL post RT. Optimal cut-off values for cf DNA were set at 10ng/mL pre-RT and 15ng/mL post RT to stratify patients into low-DNA (LDNA) and high-DNA (HDNA) groups. The pre-RT HDNA in the cohort presented with more advanced and metastatic disease. Quantitative analysis showed that the cfDNA load initially increased significantly post-RT in some patients which correlated with their good treatment outcomes as regression in tumor and disease burden as per the PET-CT scan results. Since, total cfDNA is derived by cell death associated with apoptosis and necrosis, the increase in cfDNA post RT could be due to more cell death indicating good response to RT. This effect was dose-dependent. On follow up after 2-2.5 months post completion of RT, the cfDNA levels reduced significantly with a good outcome. On the contrary, patients not showing any change in the cfDNA load post RT had less response and a progressive disease confirming a poor response to RT. Case 1: A significant change in cfDNA load was seen in a 51 yr old female with small cell neuroendocrine Lung cancer, with brain metastases and post RT HDNA which increased even after RT doses of 1500 cGy (mid treatment) and 3000 cGy (total dose) to brain. A follow up after 2.5 months post radiation, the cfDNA level came down significantly with a symptomatic reduction of the disease burden in the brain and correlated with clinical response (CR) as shown in PET scan (SUV changed from 15 to Nilot). Case 2: A 52 yrs old female diagnosed with adenocarcinoma stomach, with pre-RT cf DNA load of 10.6ng/ml showed a twofold increase after 2520 cGy of radiation and 68.8ng/ml after 5580cGy of radiation. PET-CT scan showed a regression of the size of the tumor and the disease burden. The patient when followed up after 2 months of completion of RT, the cf DNA reduced to 9.6ng/ml with significant decrease in the disease burden (SUV in PET-CT scan changed from 18.1 to Nilot).

Conclusion: The study confirms the feasibility and importance for the use of post-RT cfDNA levels as an early predictor of treatment responses for patients with solid tumors in our cohort.


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To Study The Role Of Pre-treatment MicroRNA Expression As A Predictor Of Response To Chemoradiation In Locally Advanced Carcinoma Cervix

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Purpose/Objective(s): Cervical cancer is the fourth most common cancer worldwide. External beam radiotherapy with concurrent cisplatin followed by brachytherapy is considered standard of care in locally advanced carcinoma cervix, with 50% of patients presenting with recurrence or persistent disease. At present there is no prognostic factor to predict the outcome of disease in locally advanced carcinoma cervix patients treated with standard therapy. MicroRNAs (miRNAs) are small, single-stranded noncoding RNA constituting 18-22 nucleotides. It has been shown that miRNAs are differentially expressed (upregulated or downregulated) in many cancer cells. Expression of miRNAs can be used as molecular biomarkers to predict clinical response in locally advanced carcinoma cervix patients.

Materials/Methods: In an observational study, we enrolled 32 patients of locally advanced carcinoma cervix (Stage IB-IVA) after pathological confirmation of biopsy sample from 2017-2018. Expression of six microRNA (miRNA) (miRNA-9-5p, miRNA-31-3p, miRNA-100-5p, miRNA-125a-5p, miRNA-125b-5p, miRNA-200a-5p) in formalin fixed paraffin embedded (FFPE) biopsied tissue were analyzed by real time quantitative reverse transcriptase polymerase chain reaction (RT qPCR). Pre-treatment evaluation of disease status was done with clinical examination and MRI pelvis imaging. All patients received external beam radiotherapy with concurrent chemoradiotherapy followed by brachytherapy as standard treatment. Patients were evaluated for clinical response after 3 months of completion of treatment, with clinical examination and MRI pelvis scan using RECIST 1.1 criteria. Responses were classified as complete response (CR) as disappearance of all disease in response to treatment and Non-response (NR) as patients with partial response, stable or progressive disease. Results were statistically analyzed using Mann Whitney U test to examine significant difference between expression of microRNA between patients with complete clinical response (CR) and those with non-response (NR).

Results: Out of total 32 patients, 24 patients (75%) had Complete Response and 8 patients (25%) had Non-Response to standard therapy. Out of six miRNAs, expression of miRNA-100-5p was upregulated in complete responders (CR) and downregulated in Nonresponders (NR), which showed a trend towards statistical significance (p value = 0.05). Other
Phase II Trial of Flaxseed to Prevent Acute Complications after Chemoradiation for Lung Cancer

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Purpose/Objective(s): The effectiveness of radiotherapy for thoracic malignancies is limited by acute radiation-induced complications such as radiation pneumonitis (RP) and radiation esophagitis (RE). Based on preclinical work from our lab, the present single-arm phase II trial investigated the feasibility of administering 8-9 weeks of flaxseed (FS), a whole grain with anti-inflammatory and anti-oxidative properties, as a radioprotector in patients receiving chemoradiation (RT) therapy for non-small cell lung cancer (NSCLC). Herein, we report outcomes of the primary endpoint of RP and the secondary study endpoints of RE and clinical outcomes.

Materials/Methods: Between June 2015 and February 2018, patients with locally advanced or metastatic NSCLC where definitive chemoradiation (RT) was planned were enrolled. Finely ground FS in 40-gran packets were provided to patients for daily consumption in any patient-desired formulation 1 week prior to RT and continued throughout RT as tolerated. RP and RE grades were assigned according to the CTCAE v4.0 scale.

Results: Of 33 patients enrolled, 5 patients (15%) did not receive RT, 4 (12%) withdrew after enrollment and before FS consumption, and 4 (12%) did not return a FS consumption log. The remaining 20 patients (61%) had documented RT and FS ingestion with a mean FS consumption and standard deviation of 5 ± 2.8 weeks. Baseline characteristics are described in the table. For the primary study endpoint, 1 patient (3% of all enrolled patients and 5% of patients who ingested FS), with unverifiable FS consumption, developed Grade 3 RP. Regarding secondary study endpoints, 12 patients (36%) developed Grade ≤2 RE, but no patients developed Grade ≥3 RE. 12 patients (36%) reported difficulty tolerating FS consumption.

Conclusion: Median overall survival and progression free survival for the cohort were 24 and 12 months, respectively, with no significant differences between those who did and did not consume any FS.

Table: Abs 3171: Table

<table>
<thead>
<tr>
<th>Age, mean (range)</th>
<th>All Patients (n = 33)</th>
<th>Any FS (n = 20)</th>
<th>No FS (n = 13)</th>
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<tr>
<td>Sex</td>
<td>68 (36-49)</td>
<td>69 (45-82)</td>
<td>57 (36-77)</td>
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<tr>
<td>Male</td>
<td>18</td>
<td>11</td>
<td>7</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Stage (AJCC 7th Edition)</td>
<td>31</td>
<td>18</td>
<td>12</td>
<td>0.83</td>
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<tr>
<td>I-III</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
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<tr>
<td>Dose (cGy)</td>
<td>6660 (4750-6676)</td>
<td>6660 (4862-6676)</td>
<td>6000 (4750-6672)</td>
<td>0.032</td>
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<tr>
<td>Pulmonary Function, mean (range)</td>
<td>1.96 (0.76-3.37)</td>
<td>1.69 (0.76-2.69)</td>
<td>2.29 (1.37-3.37)</td>
<td>0.043</td>
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<tr>
<td>DCF (%)</td>
<td>68 (21-130)</td>
<td>79 (21-92)</td>
<td>63 (31-130)</td>
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<td>Pack-Years, median (range)</td>
<td>50 (3-150)</td>
<td>35 (3-150)</td>
<td>38 (10-100)</td>
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</tbody>
</table>

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Tumor-related Leukocytosis Is Associated With A Suppressive Tumor Immune Microenvironment In Cancer Patients

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Purpose/Objective(s): Tumor-related leukocytosis (TRL) is correlated with poor survival in various types of cancers, but the microenvironment of TRL-associated human tumors has not been fully elucidated.

Materials/Methods: The transcriptional signatures of tumor tissues obtained from cervical cancer patients with (TRLpos) and without TRL (TRLneg) were compared. As a surrogate for TRL diagnosis, a leukocytosis signature (LS) score was derived using genes differentially expressed between TRLpos and TRLneg tumors. The immunological profiles of patients in the TCGA database with high (LShigh) or low (LSlow) LS scores were compared.

Results: TRLpos tumors were transcriptionally distinct from TRLneg tumors, exhibiting up-regulation of radioresistance and down-regulation of adaptive immune response-related genes. In the TCGA cervical cancer cohort (n = 303), patients with high LS had inferior survival rates compared to those with low LS (P = 0.023). LShigh tumors were enriched in radioresistance, wound healing, and myeloid-derived suppressor cell (MDSC) signatures and had a higher infiltration of M2 macrophages and a lower infiltration of M1 macrophages and lymphocytes. LShigh tumors also expressed higher levels of CXCR2 chemokines, CSF2, and CSF3. In the pan-cancer cohort (n = 9984), LShigh tumors also exhibited poor survival, signatures of a suppressive immune microenvironment, and higher expression of CXCR2 chemokines.

Conclusion: Our data provide evidence for a suppressive immune microenvironment in patients with TRL and suggest promising targets, such as the CXCR2-axis.

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