treatment clinical factors. This treatment-based system can help to weigh risks and benefits of contemporary treatment options.

Author Disclosure: **B.M. Aleman**: None. **S. Roshani**: None. **O. Visser**: None. **M. Schaapveld**: None. **F.E. Leeuwen**: None.

## 3334

### Artificial Intelligence for Identification of Radiation-Related Toxicities from the Electronic Health Records of Patients with Head and Neck Cancer

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**Purpose/Objective(s):** Radiotherapy-related late toxicities (RLT) impact the quality of life of head and neck cancer (HNC) patients. Progression of RLT is often subtle and its recognition is dependent on multiple visits, recorded within unstructured electronic health records (EHR). This study details the process of tuning existing Artificial Intelligence (AI) platforms to identify RLT.

**Materials/Methods:** The validated AI platform, DARWENTM, pre-trained on general clinical data, was fine-tuned and validated using data from HNC patients referred to a RLT clinic. DARWENTM employed four models: relevance model (eliminates irrelevant sentences), subject detection model (determines RLT is related to the specific patient), assertion status model (determines presence of RLT), and query model (triangulates RLT, fine-tuned to adapt the engine to the concept of interest). A rulebook defining each toxicity (dysphagia, fibrosis, osteoradionecrosis (ORN) and trismus) and the toxicity status (ground truth) was provided by a radiation oncologist. Data was split into a training and an unseen cohort. Model queries were fine-tuned using the training cohort and run against an unseen cohort to determine toxicity status. Output was validated by comparing against manually curated ground truth. The ground truth was reviewed by a second trained reviewer and discrepancies in the manually curated data were adjudicated. Models were further fine-tuned after adjudication. Overall accuracy, precision (positive predictive value), and F1 scores (harmonic mean of sensitivity and positive predictive value) were generated.

**Results:** Patients (n = 207) were split into training (n = 167) and unseen (n = 40) cohorts. Prior to adjudication, DARWEN$^{TM}$ AI achieved overall accuracy of 53% (F1 = 0.66) for all toxicities. Precision of 42% for dysphagia (F1 = 0.33), 70% for fibrosis (F1 = 0.74), 86% for ORN (F1 = 0.88) and 53% for trismus (F1 = 0.50) was achieved. After adjudication and further fine-tuning, DARWEN$^{TM}$ AI achieved overall accuracy of 87% (F1 = 0.92) across all toxicities. Precision of 92% for dysphagia (F1 = 0.88), 100% for fibrosis (F1 = 0.93), 93% for ORN (F1 = 0.93) and 94% for trismus (F1 = 0.91) was achieved. Running refined models on unseen cohort (759 notes with >1 million characters) took a mean (SD) of 4.01 (0.42) seconds for each toxicity.

**Conclusion:** This study demonstrates the feasibility and accuracy of fine-tuning existing AI to find patients experiencing RLT from EHR. For future work, AI should be tested on EHR from a real-world HNC cohort, with or without RLT. For the purposes of this study, DARWEN$^{TM}$ was fine-tuned using the entire patient EHR; in the future, less documentation could be used for continuous RLT monitoring and early detection.

Author Disclosure: **F. Alfadli**: None. **J.M. Mathew**: None. **J.N. Waldron**: None. **J.Y. Kwan**: None. **S. Aviv**: None. **M.M. Nguyen**: None. **V. Mokriak**: None. **C. Pettengell**: None. **P. Wong**: Grant/research funding; AstraZeneca, Bristol Myers Squibb. Ownership equity; MISO chip.

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### Genome-Wide Cell-Free DNA Fragmentation Analyses for Early, Non-Invasive Detection of Treatment Response to Standard of Care Adjuvant Radiation Treatment in High-Grade Gliomas

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**Purpose/Objective(s):** Biomarkers to assess response to standard chemoradiation following resection for high grade glioma (HGG) are imprecise. Assessments often require multiple MRIs months apart and fail to differentiate treatment response from progression, in a disease with median progression-free survival (PFS) around 7 months. We previously developed DELFI (DNA Evaluation of Fragments for Early Interception) to use cost-effective, low-coverage, whole-genome sequencing (WGS) and machine learning to evaluate millions of cfDNA fragments in the blood that can reflect cancer-related genomic and epigenomic changes. Here we analyze fragmentation in patients with HGG to identify noninvasive biomarkers of RT response and disease progression.

**Materials/Methods:** We enrolled 39 patients with primary HGG with 116 plasma liquid biopsies collected pre-surgery, pre-RT, 2, 4 and 6 weeks on-RT, and 1-month post-RT. We extracted cfDNA from 58 liquid biopsies (n = 17 patients, with n = 5, 16, 13, 8, 14 and 2 draws at the pre-surgery, pre-RT, 2, 4 and 6 weeks on-RT, and 1-month post-RT time points, respectively) and performed WGS of cfDNA fragments. We analyzed cfDNA fragmentation profiles by summarizing the ratio of short (100-150 bp) to long (151-220 bp) fragments in 5Mb bins genome-wide, and correlated profiles between timepoints for each patient. We estimated PFS as time between diagnosis and first indication of new treatment post-RT.

**Results:** Pre-surgery cfDNA concentrations trended higher than at pre-RT (mean 18.9 ng/mL vs. 9.7 ng/mL) and further decreased on-RT and post-RT (mean 5.9 and 5.6 ng/mL, respectively). Fragmentation profiles pre-RT were more correlated to on-RT profiles than to pre-surgery profiles (median correlation 0.94 vs. 0.88), possibly reflecting high pre-surgery tumor burden that falls after resection and adjuvant treatment. At four weeks on-RT, a higher correlation to the pre-RT fragmentation profile was associated with longer PFS (p = 0.01, median PFS 15.6 vs. 4.8 months for patients with correlations above and below the mean, respectively), suggesting that patients with fragmentomes resembling their lowest tumor burden profile survive longer before progression.

**Conclusion:** We provide early evidence that genome-wide cfDNA fragmentation profiles reflect relative HGG tumor burden, and that changes to fragmentation may capture early molecular signs of progression. These changes are detectable on-RT and post-RT and are associated with PFS in as few as four weeks on-RT. This interim analysis demonstrates the utility of cfDNA fragmentomes for noninvasive monitoring of treatment response in patients with HGG. We are continuing patient accrual, sample collection and sequencing (goal n = 100 patients enrolled) with the objective of identifying response biomarkers to support real time treatment modification.

Author Disclosure: **A.V. Annapragada**: Copyright/Patent/License/Royalty; Delfi Diagnostics. **A. Bartolomucci**: None. **S. Short**: None. **K. Boyapati**: None. **A. Li**: None. **D. Roche**: None. **S. Patterson**: None. **D. Bruno**: None. **D. Kaplin**: None. **C. Jackson**: Grant/research funding; Biohaven, InCephalo, Grifols. Ownership equity; Egret Therapeutics. Stock; Amgen. Co-founder with equity interests; Egret Therapeutics. **J. Weingart**: None. **K.J. Redmond**: Grant/research funding; Elekta AB, Accuray, Icotec, Canon.