

SIGNIFICANCE OF FINDINGS: The lack of knowledge of pharmacogenomic variation in African populations contributes to ethnic disparities in patient outcomes. This study addresses this gap by adding to our comprehension of variants in clinically relevant genes, giving insight into underlying mechanisms of ethnicity-based drug responses.

74325

Vast sex-specific differences in transcriptional landscapes of pancreatic neuroendocrine tumors*

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ABSTRACT IMPACT: Here, we describe extensive sex-specific differences in the transcriptomes of pancreatic neuroendocrine tumors (PNETs). Given that the clinical course of PNETs differs by sex (female sex is associated with better survival), achieving a greater understanding of the specific molecular sexual dimorphisms is invaluable for advancing personalized treatment. **OBJECTIVES/GOALS:** Epidemiologic studies demonstrate that pancreatic neuroendocrine tumors (PNETs) exhibit sexual dimorphisms with regards to prognosis, disease recurrence, and complication rates. We sought to compare the transcription and DNA methylation landscapes of PNETs by sex, to elucidate molecular differences that may underlie this sex disparity. **METHODS/STUDY POPULATION:** RNAseq data was generated from PNETs surgically resected at our institution (9 Female; 12 Male patients). RNA was extracted with the RNeasy Mini Kit, stranded sequencing libraries were prepared with TruSeq, and paired end sequencing was done on the HiSeq 2500/4000 systems. Transcript-level quantification was performed with salmon, and DESeq2 was used for differential expression analysis. To account for significant variation due to covariates other than sex, surrogate variables were computed with the SVA package and adjusted for. The goseq package was used for gene set over representation analysis. Matched DNA methylation (DNAm) and RNAseq data was downloaded from GEO (16 F; 16 M). Raw DNAm data was processed with minfi. Differential methylation analysis was done with limma and bumpHunter. Analysis was done in R. **RESULTS/ANTICIPATED RESULTS:** We found that 826 autosomal genes were differentially expressed (DE) by sex in PNETs (at FDR ≤ 0.1). Gene set over representation analysis performed on the DE genes revealed significant enrichment for several processes, including 'ascorbate & aldarate metabolism' and 'positive regulation of ERK1 & ERK2 cascade' (all FDR ≤ 0.1). When we compared DNAm profiles between sexes, we found 8 CpGs which were differentially methylated by sex (at FDR ≤ 0.1), 7 of which were proximal to genes. Methylation of one of the sex-associated CpGs, overlapping the gene TIMM8B, was found to be negatively correlated with gene expression ($\rho = -0.41$; p -value=0.02). Interestingly, TIMM8B deletion has been previously reported in other non-pancreatic neuroendocrine tumors. There were no differentially methylated regions between sexes. **DISCUSSION/SIGNIFICANCE OF FINDINGS:** Our findings demonstrate that PNETs exhibit extensive sexual dimorphisms with regards to gene expression profiles but have largely congruent methylomes by sex. These molecular differences may contribute to the variability in clinical course between men and women, and their characterization is vital for the advancement of personalized medicine.

Dissemination and Implementation

82786

Quantification of the Accuracy of Stereotactic Radiosurgery using Surface Guided Imaging with 3D Printed Head Phantoms

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ABSTRACT IMPACT: This work assesses clinical implementation of a surface guided imaging system to improve the accuracy radiation delivery for treatment of brain lesions using a patient CT derived head phantom. **OBJECTIVES/GOALS:** Advancements in radiotherapy design have made clinical demand for efficient and accurate methods to deliver stereotactic radiosurgery (SRS) for treatment of intracranial lesions. This study assesses the potential of using surface guided imaging for setup using a 3D patient specific head phantom. **METHODS/STUDY POPULATION:** A single isocenter, multiple metastases SRS plan was generated on a CT derived RTsafe Prime phantom made of tissue equivalent materials and a polymer gel insert. Five targets of varying diameters were treated with 8Gy of radiation using two different positioning techniques. The first gel insert was irradiated within the phantom according to internal alignment with standard orthogonal x-ray imaging while the second setup used surface guided imaging, based on external anatomy. 42 hours after irradiation, the phantom was scanned in a head coil using a 1.5T MRI. MR images were fused with the patient CT data and structure set to further evaluate calculated and measured dose distributions. **RESULTS/ANTICIPATED RESULTS:** Discrepancies in phantom setup according to standard orthogonal x-ray imaging compared to surface guided imaging demonstrated to be <1mm in each translational (vertical, longitudinal, and lateral) and angular (rot, roll, pitch) directions. The 3D gel inserts permitted spatial analysis to compare dose distributions of measured values to those calculated in a treatment planning system (TPS). 3D GI (Gamma Index) analysis showed good alignment in high dose regions and resulted in passing rates >94% (5%/2mm) and >87% (3%/2mm). Finally, 3 of 5 targets showed better 3D GI passing rates and less geometric offset for positioning with the surface guided imaging. **DISCUSSION/SIGNIFICANCE OF FINDINGS:** 3D spatial analysis of human like phantoms demonstrated that patient positioning according to external anatomy performed comparable to standard methods aligning to the internal anatomy, for a multiple met SRS treatment.

97856

Implementation of DPYD and UGT1A1 pharmacogenetic testing to guide chemotherapy dosing

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ABSTRACT IMPACT: The implementation of DPYD and UGT1A1 pharmacogenetic testing, a promising tool of precision medicine,