Quantitative Textural Analysis (QTA) in CT imaging: identifying markers for genetic instability and overall survival in cohort of previously treated metastatic pancreatic cancer (mPC)

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INTRODUCTION

Metastatic pancreatic cancer (mPC) is a rapidly fatal disease with limited treatment options that often carries bleak prognosis. Developing non-invasive tools to identify pancreatic tumor characteristics would aid in optimizing available treatments. Tumors with high numbers of dsDNA breaks identified as intrachromosomal copy number aberrations via CGH are often more susceptible to DNA-damaging chemotherapeutics. Identifying these tumors using standard-of-care CT imaging would allow targeted treatment to begin sooner.

AIMS

Quantitative textural analysis (QTA) is used to describe indiscernible CT imaging features that correspond to tumor microenvironment, vascularity, and local heterogeneity **[Figure 1]**. Reliable CT QTA parameters indicative of treatment options and prognosis have been developed for HCC, GBM, NSCLC, and colorectal cancer. The aim of this exploratory study was to identify QTA features that correlated with dsDNA breaks. We also sought to explore the prognostic value of QTA features in tumors and normal pancreatic tissue.

Quantitative Textural Analysis

TexRAD is a proprietary software-based QTA platform that measures pixel signal from multiple imaging modalities obtained during standard of care scans such as MRI, CT, and PET. Results are then displayed using a Histogram Frequency Curve (HFC) that varies based on the heterogeneity of the tumor **[Figure 2]**. HFCs are generated by separating pixels (ssf) into fine (ssf=1-2), medium (ssf=3-4), or coarse (ssf=5-6) clusters using Laplacian of Gaussian filtering. HFCs of each tumor haven been correlated with biologic markers of hypoxia, proliferation, neovascularity, and other characteristics.

Figure 1. QTA Application

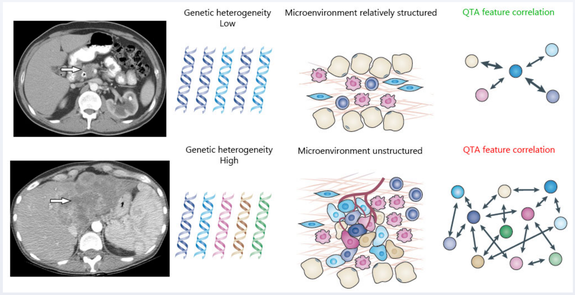

Figure 1. Quantitative textural analysis (QTA). Spatial information is derived from regional differences in enhancement and density. Textural features that correspond to tumor microenvironment, vascularity, and local heterogeneity are described using QTA. It is hypothesized that these phenotypically dependent QTA features can be linked to genotypic endpoints like chromosomal instability.

METHODS

Metastatic mPC sites were biopsied and molecularly profiled. 85% of the cohort had 1-3 previous treatment regimens, and the remaining 15% had 4-6. Intrachromosal copy number were assessed by CGH in tumor specimens. Patients were treated with commercially available cytotoxic regimens based on these individual molecular profiling results. Patients with available pre-biopsy abdominal portal-venous phase CT scans were obtained for retrospective analysis. There were 9 males and 6 females all with stage IV cancer from 34 – 71 years old (median 59) **[Figure 5]**. Analysis of pre-biopsy pancreas imaging was performed by drawing regions of interest around the primary pancreas adenocarcinoma (n=15) and the normal pancreas tissue when available (n=12). QTA parameters were derived using the TexRAD platform at texture filtering densities of medium (ssf=3) and coarse (ssf=5). These values were compared to intrachromosomal copy number aberrations per tumor and overall survival post-treatment using a Spearman's rank correlation coefficient.

Figure 2. Histogram Frequency Curve

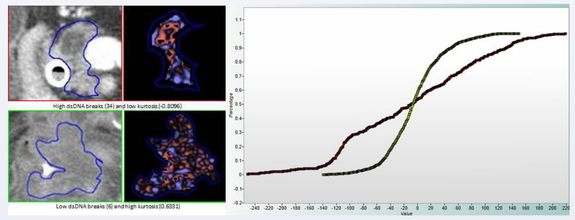

Figure 2. Representative imaging for kurtosis and dsDNA breaks with Histogram Frequency Curve (HFC). Imaging of a tumor region with low kurtosis and high dsDNA breaks (*top image left, red curve*) versus high kurtosis and low dsDNA breaks (*bottom image left, green curve*). Histogram frequency curve to right generated based on post-filtered pixels in tumor region.

RESULTS: dsDNA BREAKS

Quantity of dsDNA breaks in tumor tissue correlated with more negative kurtosis values of the primary tumor mass using medium texture filtering (p = 0.034, n = 15, ssf=3) **[Figure 3].**

Figure 3. dsDNA Breaks vs. Kurstosis

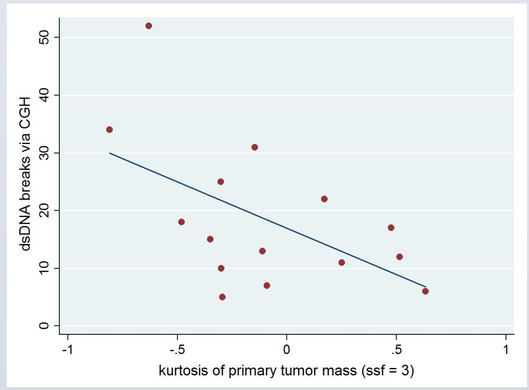

Figure 3. Scatterplot and regression line of dsDNA breaks vs. kurtosis of tumor mass using medium filtering (ssf=3). Negative (low) kurtosis was significantly correlated with higher numbers of dsDNA breaks identified via CGH of tumoral biopsies (p = 0.034, n = 15).

RESULTS: OS

Exploratory analysis with coarse texture filtering yielded a correlation between reduced overall survival in clinical trials and increasing entropy of the normal pancreas (p = 0.0014, n = 12, ssf=5) **[Figure 4].** Analysis of the tumor QTA features in relation to prognostic factors were not significant.

Figure 4. OS vs. Entropy

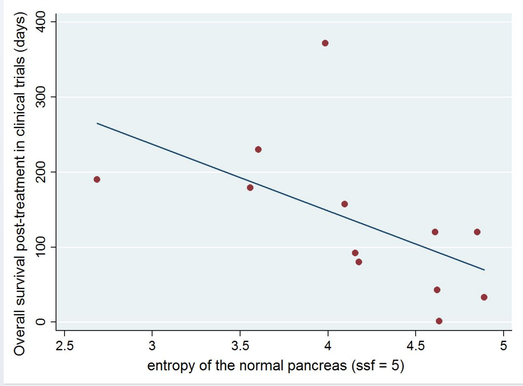

Figure 4. Scatterplot and regression line of OS in clinical trials vs. entropy of the normal pancreas using coarse filtering (ssf=5). High entropy was associated with diminished overall survival (p = 0.0014, n = 12).

Figure 5. Patient Characteristics

Patient ID	Age at biopsy	dsDNA breaks	CA19-9	Gender	Kurtosis (ssf = 3)	Entropy (ssf = 5)	OS in clinical trials (days)
4	42	10	13956	M	-0.2998	4.63472	190
5	59	11	-	F	0.2508	2.68595	1
6	34	52	12078.5	M	-0.6294	-	42
14	70	18	1885.3	F	-0.4815	4.1549	120
22	54	13	298.6	M	-0.1113	3.60496	43
27	64	5	34.2	M	-0.2943	4.17554	120
32	61	12	352.1	F	0.5158	4.62214	179
33	67	22	3063	M	0.1711	4.0961	92
35	56	25	-	F	-0.3023	3.98503	80
36	56	17	-	M	0.4753	4.89092	372
38	64	6	1191	M	0.6331	3.5582	33
42	65	15	-	F	-0.3489	4.84989	230
45	53	31	539.9	M	-0.1463	-	161
48	46	7	443796	F	-0.0902	-	-
49	71	34	14367	M	-0.8097	4.61173	157
median	***59***	***15***	***1885.3***	**-**	***-0.1463***	***4.16522***	***120***

Figure 5. Table of patient characteristics. All patients had stage IV treatment-resistant mPC when enrolled into clinical trials. There were 9 males and 6 females with a median age of 59 years old. Median survival post-treatment was 120 days.

CONCLUSION

This exploratory study with admittedly limited sample size raises interesting possibilities about the use of QTA parameters as diagnostic tools and/or biopsy adjuncts in assessing pancreatic adenocarcinoma susceptibility to commercially available cytotoxics. Secondarily, entropy, a potential marker of heterogeneity and inflammation in the normal pancreas, represents an intriguing possibility for gauging prognosis in mPC.

ACKNOWLEDGEMENTS

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