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A Phantom Study to Investigate Robustness and Reproducibility of Grey Level Co-Occurrence Matrix (GLCM)-Based Radiomics Features for PET

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Supplemental Table

Table S1. Relationships of textural features with tumor heterogeneity for different parameters and methods.

Study (group)	# of Patients	Machine	Cancer Type	Reconstruction and Smoothing	Dose and Tracer	Metrics	Quantisation	Segmentation	Direction	Tumor Size (baseline)	Tumor Size (after treatment)	Prediction of Response
Hatt (2011). INSERM France [1]	25	Biograph PET/CT Siemens	Non-small cell lung cancer	Ordered subsets maximization algorithm (4 iterations, 8 subsets). Attenuation correction using CT data.	45–60 min after injection	Measuring using COV, lobectomy, CT images, MATV		2 manual delineations on CT, I_{50}, adaptive (Nestle) and FLAB				Relationship between volumes and impact of size and uptake in heterogeneity
Tixier (2011). INSERM France [2]	41	PET/CT Gemini; Phillips	Esophogeal	3D row action maximum likelihood algorithm (2 iteration, relaxation 0.05 & 3D gaussian post filtering of 5 mm in FWHM)	5 MBq/kg, avg. 54 min after injection	SUV, intensity histogram, voxel alignment matrix, intensity—size zone matrix, co-occurrence, neighbourhood intensity-difference matrix. ROC curves	16, 32, 64,128 discrete values. 64 is subsequently used	Primary was first identified by experienced nuclear medicine physician and then delineated automatically using fuzzy locally adaptive Bayesian algorithm (FLAB)	13 different angular direction			Homogeneity and entropy significantly differentiate between non-responders with others (partial or complete responders). No significant differences between
Tixier (2012). INSERM France [3]	16	PET/CT Gemini; Phillips relaxation parameter 0.05	Esophogeal		2 min acquisition time, 60 min after injecting 6 MBq/kg	8 parameters for histogram, 17 for co-occurrence/intensity-size zone	8,16,32,64,128	Primary was first identified by experienced nuclear medicine physician and then delineated automatically using fuzzy locally adaptive	13 different angular direction	Larger than 10 cm^3	Reproducibility study (Entropy is the most reproducible). Entropy, homogeneity and dissimilarity	

								Bayesian algorithm (FLAB)			are preferred features
Hatt (2013). INSERM France [4]	50	Philips Gemini PET/CT	Locally advanced oesophageal	-CT attenuation correction -3D row-action maximum likelihood algorithm (2 iterations, relaxation parameter 0.05, 5 mm 3D Gaussian post filtering, 4 × 4 × 4 voxel grid sampling)	5 MBq/kg 60 min before scan	AUC-CSH -only those shown as robust for different reconstruction, acquisition &reproducibility -entropy, homogeneity, dissimilarity, intensity variability, size-zone variability, zone percentage, high intensity emphasis. (preferred) Correlations assessed using Pearson's correlation coefficient Bland-Altman assessed variability of image derived parameter AUC-ROC		Delineated in 3 ways: 42% of SUV_{max} threshold; adaptive threshold accounted for tumor/background difference; Fuzzy locally adaptive Bayesian (FLAB)			Heterogeneity parameter more dependent on delineation than PVC. Entropy and homogeneity were robust to delineation and PVC
Tixier (2014). INSERM France [5]	102	Philips Gemini PET/CT	Non-small cell lung cancer	CT-based attenuation correction and a 3D row-action maximum likelihood algorithm with a previously optimized protocol (2	3D PET data were subsequently acquired with 2 min per bed position for 60 min ^{18}F-FDG (5 MBq/kg; 425 ± 95;		A 64-gray-level quantization was used.	FLAB was exploited in this work using 2 or 3 classes to adequately cover the entire MATV, including low-uptake regions.	Local features were computed over 13 directions	Primary tumors with a MATV larger than 3 cm^3	Change of size is not explicitly reported. Homogeneity, entropy and dissimilarity

				iterations; relaxation parameter, 0.05; 5 mm in full width at half maximum 3D Gaussian post filtering; 4 × 4 × 4 mm voxels grid sampling)	range, 223–690)				
Hatt (2015). INSERM France [6]	555							FLAB	
Kidd (2008). Washington [7]	72	Hybrid PET/CT scanner (Biograph LSO 2, Siemens Medical Solutions)	Cervical cancer	Ordered-subset expectation maximization (subset and iteration are not mentioned) post reconstruction Gaussian filter (5 mm full width half maximum)	42–120 min (median, 65 min) after the administration of 15–20 mCi FDG, with imaging times of 2–4 min/bed position	H (dV/dT) is heterogeneity		40% threshold	3 months after treatment. Change of size is not explicitly reported
Brooks (2011). Washington [8]	73	Hybrid PET/CT scanner (Biograph LSO 2, Siemens Medical Solutions)	Cervical cancer	Ordered-subset expectation maximization (subset and iteration are not mentioned) post reconstruction Gaussian filter	42–120 min (median, 65 min) after the administration of 15–20 mCi FDG, with imaging times of 2–4 min/bed	The standard deviation, skewness and kurtosis	8 bit	40% threshold	Change of size is not explicitly reported

				(5 mm full width half maximum)	position				
Brooks (2013). Washington [9]		Hybrid PET/CT scanner (Biograph LSO 2, Siemens Medical Solutions)	Cervical cancer	Ordered-subset expectation maximization (subset and iteration are not mentioned) post reconstruction Gaussian filter (5 mm full width half maximum)	42–120 min (median, 65 min) after the administration of 15 to 20 mCi FDG, with imaging times of 2 to 4 min/bed position	New heterogeneity metric the sphericity, extent, Shannon entropy (S) and the accrued deviation from smoothest gradients (ζ) as image heterogeneity metrics	40% threshold		Compared against experienced expert
Brooks (2013). Washington [10]	85	*n* = 58 Siemens Biograph 2 *n* = 27 Siemens Biograph 40	Cervical carcinoma	*n* = 58 OSEM 8 sets 2 iterations and 5.3 mm post reconstruction Gaussian smoothing *n* = 27 OSEM 8 sets 4 iterations and 4 mm post reconstruction Gaussian smoothing (9 most recent Biograph 40 image sets underwent an additional point-spread	The maximum SUV of the tumors analysed ranged from 4 to 56 and approximately followed a log-normal distribution with median of 13 and variance of 74	New heterogeneity metric the sphericity, extent, Shannon entropy (S) and the accrued deviation from smoothest gradients (ζ) as image heterogeneity metrics	40% threshold (The oncologist then made slight manual adjustments to the ROI to remove any obvious non-tumor pixels such as those comprising bladder or bowel regions)	Size was not explicitly mentioned	

				function/time-of-flight correction)							
Brooks (2015). Washington [11]	27 patients as well as simulation	Siemens Biograph 40	Cervical carcinoma	OSEM 8 sets 4 iterations and 4 mm post reconstruction Gaussian smoothing (9 most recent Biograph 40 image sets underwent an additional point-spread function/time-of-flight correction)		Dissimilarity, homogeneity, energy and entropy	8-bits (i.e., 256 gray levels)	40% threshold for original data. Repeated with 50% threshold to compare with the simulated data	26 different angular direction		After 3 months
Orlhac (2014). France [12]	150 lesions of 106 patients [28 (metastatic colorectal cancer (MCC)) 24 (NSCLC) 54 (breast can-	MCC—Discovery LS System. NSCLC and BC: Gemini TF PET/CT	MCC, NSCLC and BC	MCC—OSEM with 2 iter 28 subsets and Gaussian post filtering (FWHM = 5.45 mm). NSCLC and BC: BLOB-OS-TF with 2 iter and 33 subsets				Adaptive thresholding and 40% fixed threshold		VOI greater than 5 mL used for texture analysis (77 voxels for MCC and 78 voxels for NSCLC and BC). MCC > 5.0030 cm^3. NSCLC and BC > 4.9920 cm^3.	

	cer)]							
Cheng (2013). Taiwan [13]	70	60 × Discovery ST 16 Scanner (GE Healthcare). 9 × Biograph mCT scanner (siemens Medical Solutions	Orapharyngeal squamous cell carcinoma (Head & neck)	Attenuated with CT images Ordered-subset expectation maximization (discovery:4 & 10; biograph 2 iterations, 21 subsets)	-imaged 50 min after injection -370 to 555 MBq	SUV histogram analysis, GLCM, NGTDM, -Spearman correlation coeff.,	4, 16, 32, 64	PMOD 3.3 software package
Galavis (2010). Wisconsin [14]	20	PET/CT	Adrenal gland carcinoma, lung, epiglottis, oesophagus	Ordered subset expectation maximization algorithm (4 iterations, 14 subsets × 2). Attenuation correction using CT data.	10 mCi	8 first order, 23 co-occurrence, 11 grey level run length matrix, 5 neighbouring grey level, 3 neighbourhood grey tone difference matrix		
Willaime (2013). Hammersmith. London [15]	15	ECAT 962/HR+ scanner (CTI/Siemens)	Breast cancer	OSEM iterative reconstruction method (360 iterations, 6 subsets). Filtered back projection to validate results	153–381 MBq, for 95 min	-SUV, Coefficient of variation, Skewness, Entropy, area under a cumulative histogram curve, GLCM, GLSZM, NGTDM, Homogeneity, Complexity. -Normality of relative distances assessed using Shapiro-Wilk. -Limits of repeatability were calculated.	31 discrete frames	Regions of interest were drawn manually

Leijenaar (2013). Test-retest. Netherland [16]	11 (for test retest cohort). 23 (inter-observer cohort)	ECAT Exact HR1 for test-retest. SOMATOM Sensation 16 ECAT ACCEL for other cohort	NSCLC	-normalization and attenuation weighted ordered subset expectation maximization (2 iteration, 16 subsets)	FDG	Gray level co-occurrence (GLCM), gray level run-length (GLRLM) and gray level size-zone texture matrices (GLSZM)	Equally spaced bins of 0.5 units of SUV	50% for test retest cohort. Manual delineation for other cohort	26 different angular direction			Test-retest and inter observer
Lopez (2015). Spain [17]	38	Discovery STE 16 PET CT	NSCLC	OSEM with manufacturer recommended parameters	FDG (370 MBq)	Energy, entropy, contrast, correlation and homogeneity are calculated using GLCM		SUV greater than 2.5	13 different angular direction			Relationship between heterogeneity, metabolic parameters and pathologic staging
El Naqa (2009) [18]	14/9	PET/CT Siemens biograph	Cervix/head & neck	Ordered subset' expectation maximization algorithm		SUV, Intensity-volume histogram, co-occurrence, shape based, spearman's rank. ROC curve						

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