

## Supplemental material

Table 1. MATV statistics for the entire database and per cancer site

Tumors	All	Breast (Paris Saint Louis University Hospital, France)	Cervix (Liège University Hospital, Belgium)	Esophageal(Brest University Hospital, France)	Head & Neck (Brest University Hospital, France [N=73] and McGill University Health Center, Canada [N=66])	Lung (NSCLC) Poitiers University Hospital, France
N=	555	158	45	112	139	101
MATV						
Range	3-415	3-389	6-194	3-140	3-240	3-415
Mean	35	24	57	25	32	58
Median	19	11	41	15	20	34
SD	50	49	42	27	33	77

Table 2. List of other textural features and reasons for not including them.

<b>Textural Feature</b>	<b>Insufficient reproducibility</b>	<b>Insufficient robustness vs. delineation or PVE</b>	<b>Highly correlated (<math>r_s &gt; 0.8</math>) with another TF already included in the analysis</b>
<b>2<sup>nd</sup> Angular Moment (SAM)</b>	-	-	✓
<b>Correlation (C)</b>	✓		
<b>Homogeneity (H)</b>	-	-	✓
<b>High Intensity Emphasis (HIE)</b>	-	✓	
<b>Intensity Variability (IV)</b>	-	✓	
<b>Large Zone Emphasis (LZE)</b>	✓		
<b>Size Zone Variability (SZV)</b>	-	✓	

Table 3: NSCLC patients characteristics

Characteristic		No. of patients (%) (N=101)
Sex	Male	79 (78)
	Female	22 (22)
Age (y)	Range	48-84
	Median $\pm$ SD	64 $\pm$ 8.9
Smoker	No	15 (15)
	Yes	86 (85)
Treatment	Surgery only	18 (18)
	Chemotherapy only	12 (12)
	Radiotherapy only	0 (0)
	Surgery + chemotherapy	20 (19)
	Chemotherapy + radiotherapy	42 (41)
	Chemotherapy + radiotherapy + surgery	9 (9)
Clinical stage	I	17 (17)
	II	30 (29)
	III	54 (54)
	IV	0 (0)
Histology	Adenocarcinoma	52 (52)
	Squamous cell carcinoma	49 (48)

Table 4: Esophageal patients characteristics

Characteristic		No. of patients (%) (N=112)
Sex	Male	22 (20)
	Female	90 (80)
Age (y)	Range	43-85
	Median $\pm$ SD	66 $\pm$ 10.1
Smoker	No	23 (20)
	Yes	89 (80)
Treatment	Chemotherapy + radiotherapy	44 (39)
	Chemotherapy + radiotherapy + surgery	68 (61)
Clinical stage	I	12 (11)
	II	41 (36)
	III	59 (53)
	IV	0 (0)
Histology	Adenocarcinoma	63 (56)
	Squamous cell carcinoma	49 (44)

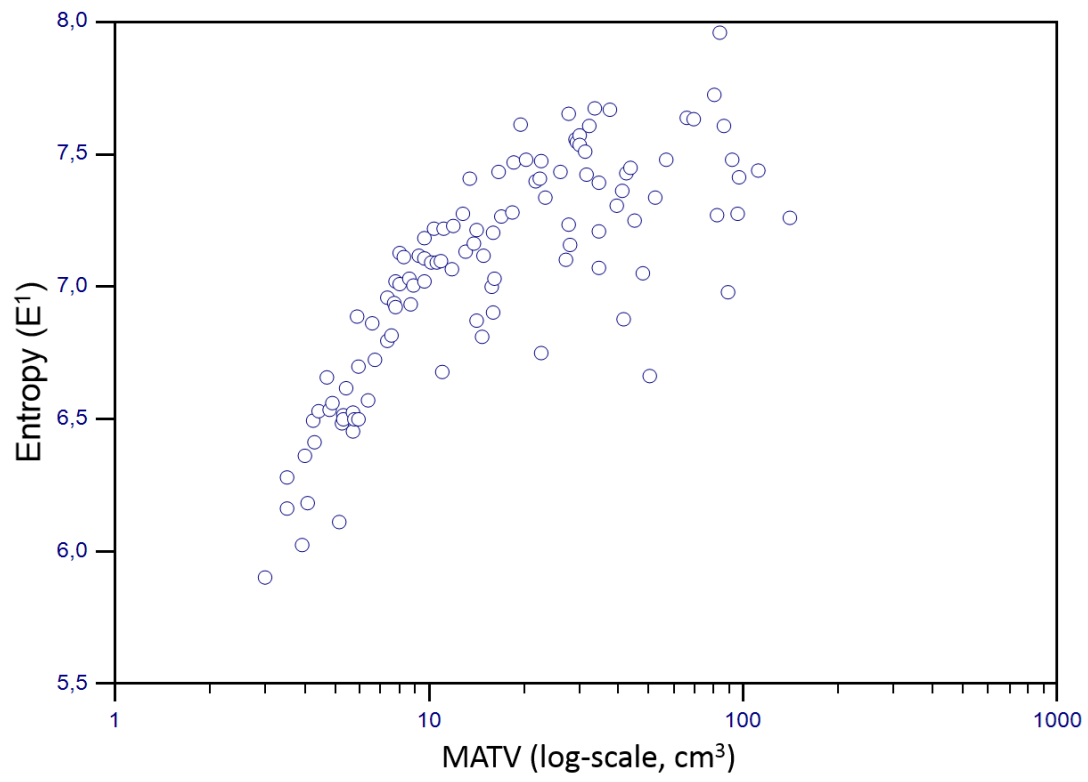
Table 5: K-M analysis full results in the esophageal cohort: comparison of hazard ratios between lower and higher risk groups, when using tumor volume and heterogeneity alone or when combining them (see also figure 7A).

Parameters	Log rank test		Group 1 (lower risk)				Group 2 (higher risk)				Hazard ratio	
	chi-squared	p-value	<i>N</i>	# deaths (%)	OS (mo)	95% CI	<i>N</i>	# deaths (%)	OS (mo)	95% CI	HR	HR 95% CI
MATV >15 cm <sup>3</sup>	4.3	0.0375	47	25 (53%)	25	16-49	65	43 (66%)	13	10-21	1.66	1.03-2.67
D <sup>1</sup> <13.9	7.8	0.0052	59	31 (53%)	23	15.6-49	53	37 (70%)	11	8-17	1.92	1-18-3.13
MATV & D <sup>1</sup>	9.2	0.0024	64	34 (53%)	23	17-49	48	34 (71%)	10	8-14	2.02	1.22-3.34

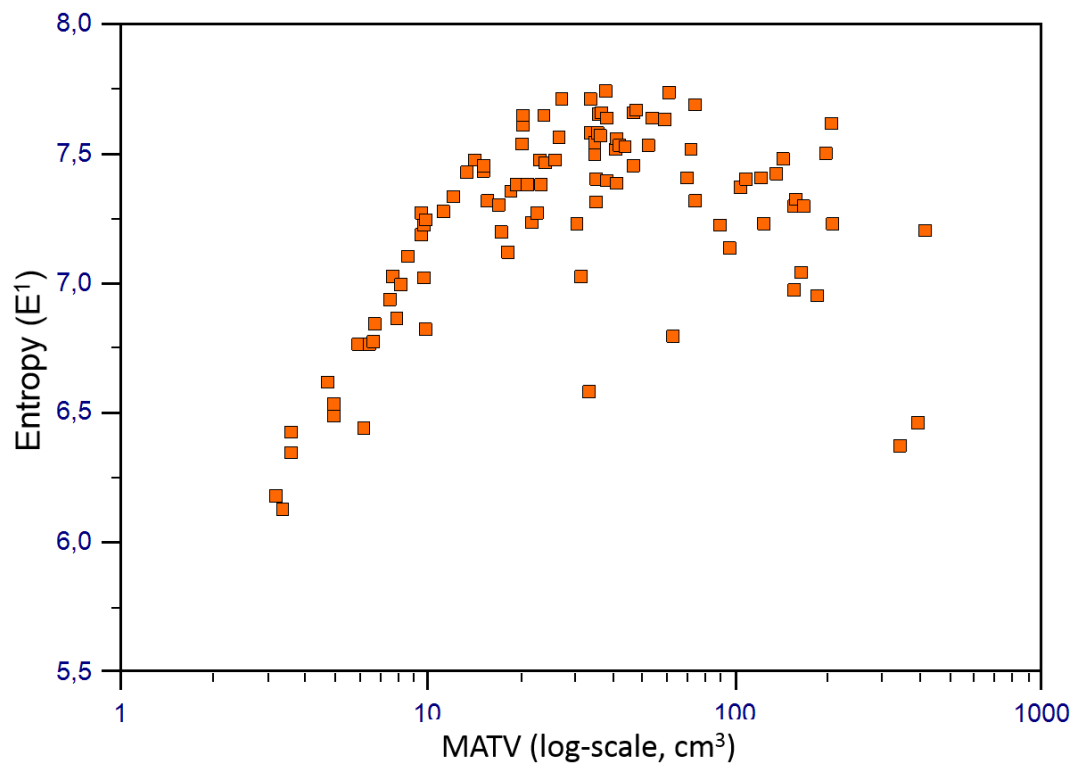
Table 6: K-M analysis full results in the NSCLC cohort: comparison of hazard ratios between lower and higher risk groups, when using tumor volume, heterogeneity and stage alone or when combining them (see also figure 7B).

Parameters	Log rank test		Group 1 (lower risk)				Group 2 (higher risk)				Hazard ratio	
	chi-squared	p-value	N	# deaths (%)	OS (mo)	95% CI	N	# deaths (%)	OS (mo)	95% CI	HR	HR 95% CI
Clinical stage (I+II vs. III)	10	0.0016	47	22 (47%)	-	-	54	40 (74%)	14.5	10.5-18.4	2.25	1.36-3.70
MATV (>35 cm <sup>3</sup> )	16.9	<0.0001	48	21 (44%)	49	20.2-49	53	41 (77%)	13.1	9-17.6	2.82	1.70-4.68
E <sup>1</sup> (>0.735)	4.8	0.011	50	25 (50%)	27.9	15.6-49	51	37 (73%)	14.3	10.7-19.1	2.09	1.20-3.62
MATV & stage	18.8	<0.0001	66	33 (50%)	25.1	19.1-49	35	29 (83%)	9	6.5-14.9	2.84	1.58-5.10
MATV & E <sup>1</sup>	29.1	<0.0001	62	28 (45%)	49	20.5-49	39	34 (87%)	9.1	6.9-14.3	3.55	2.01-6.28
MATV & stage & E <sup>1</sup>	31.8	<0.0001	74	37 (50%)	25.1	19.1-49	27	25 (93%)	7.5	4-14.1	3.81	1.90-7.63

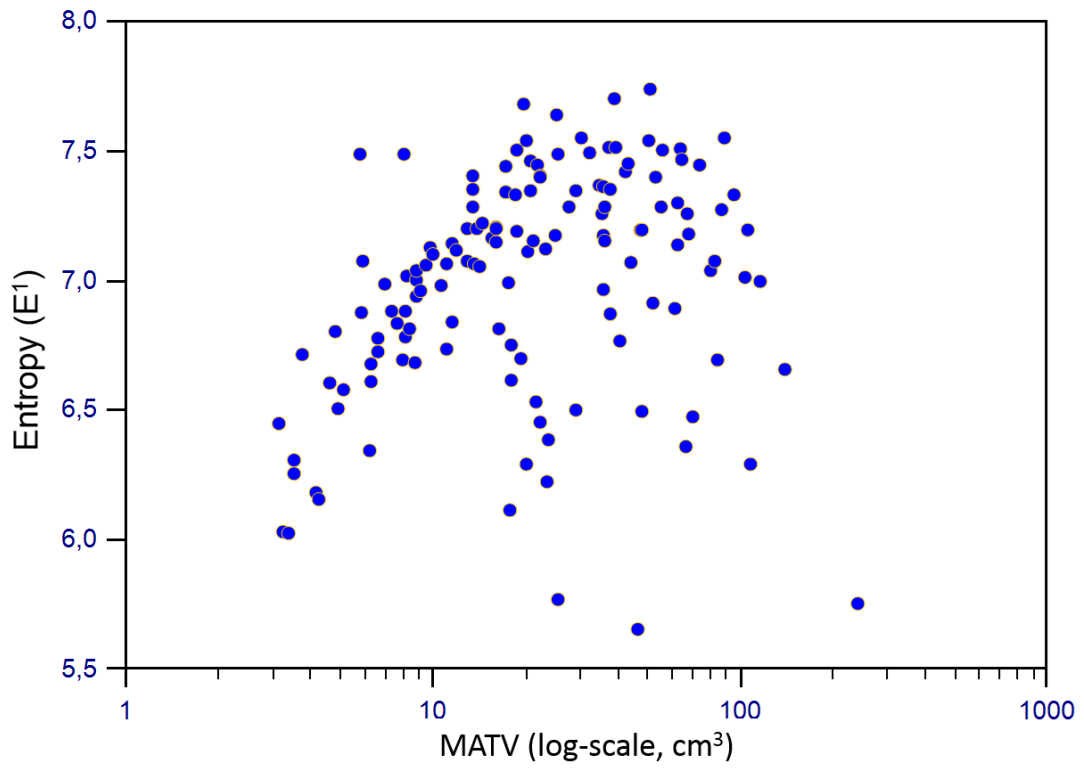
A



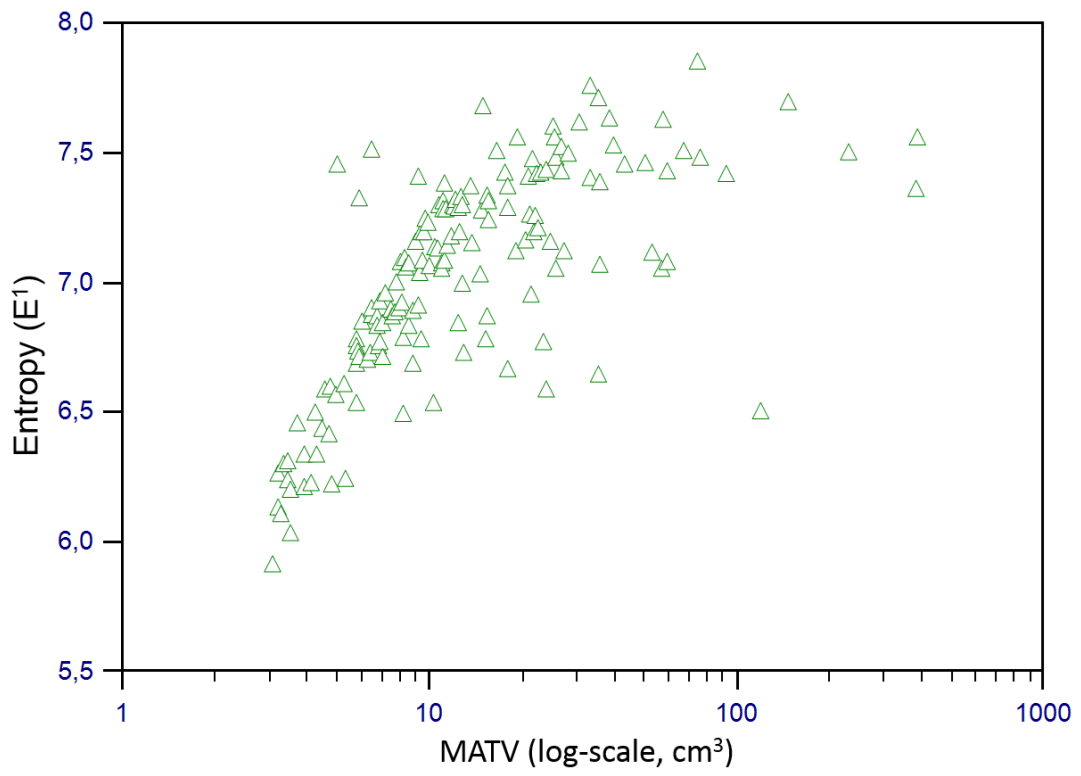
B



C



D





E

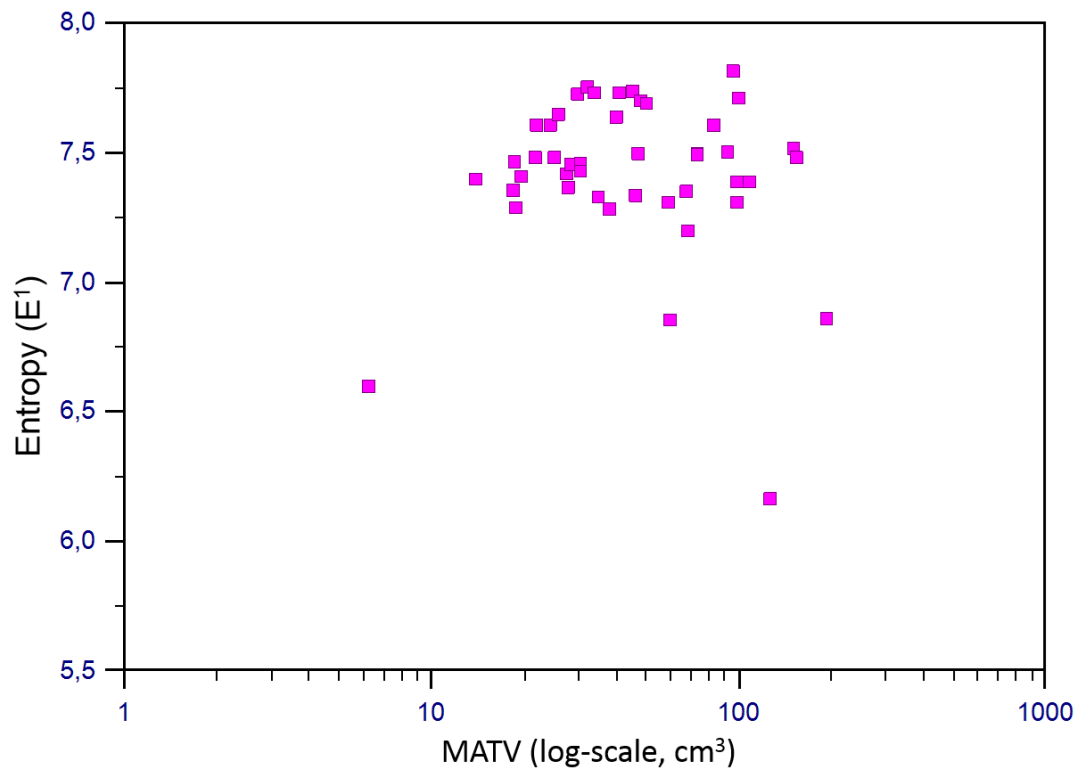
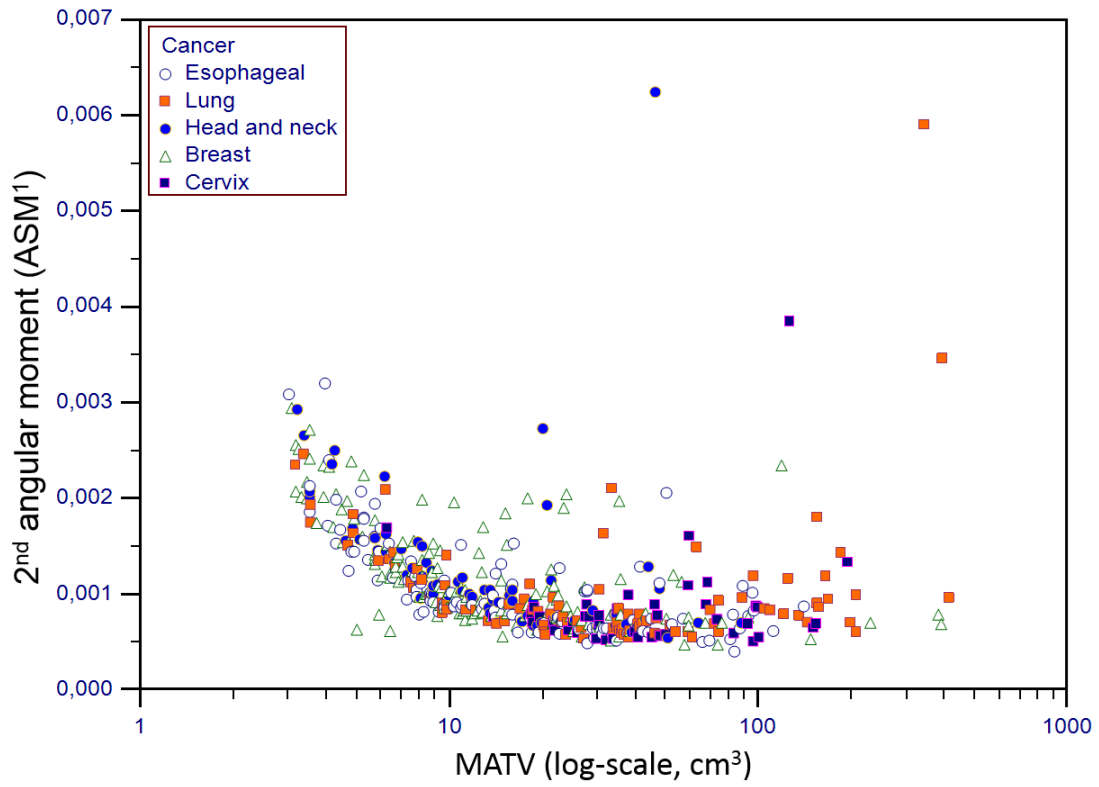


Figure 1

A



B

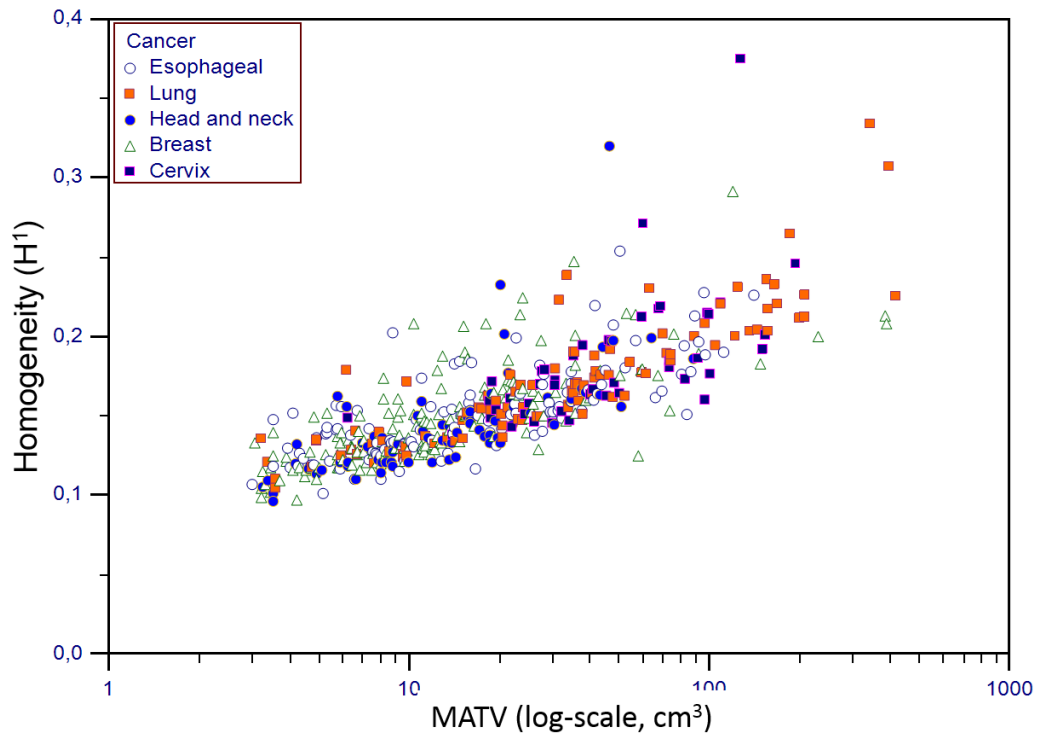
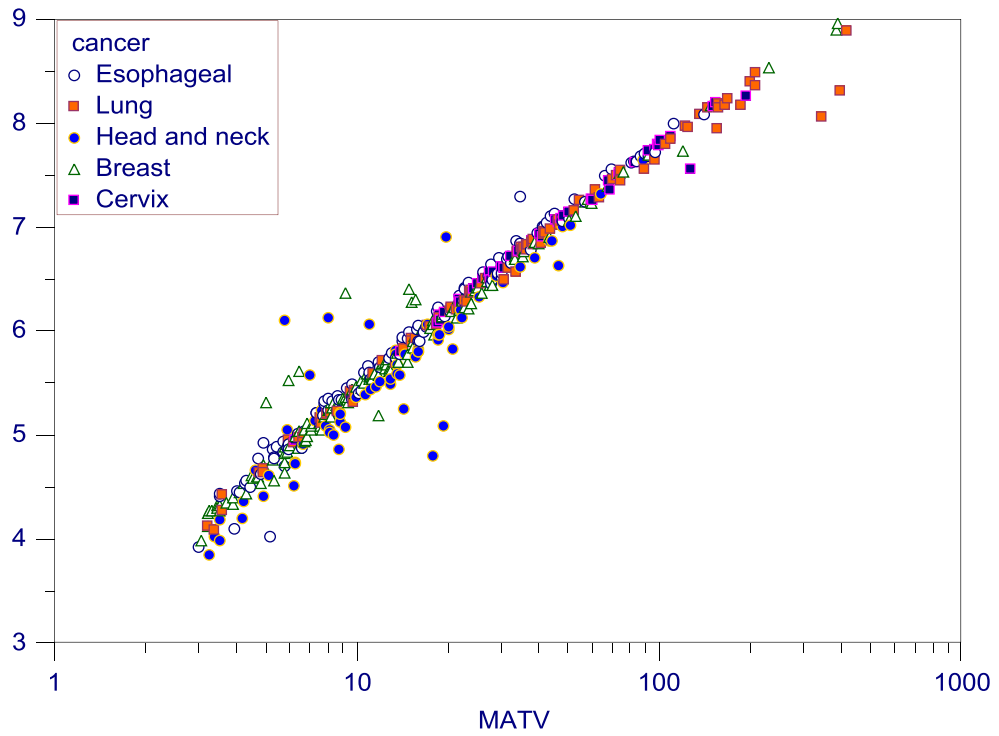


Figure 2

A



B

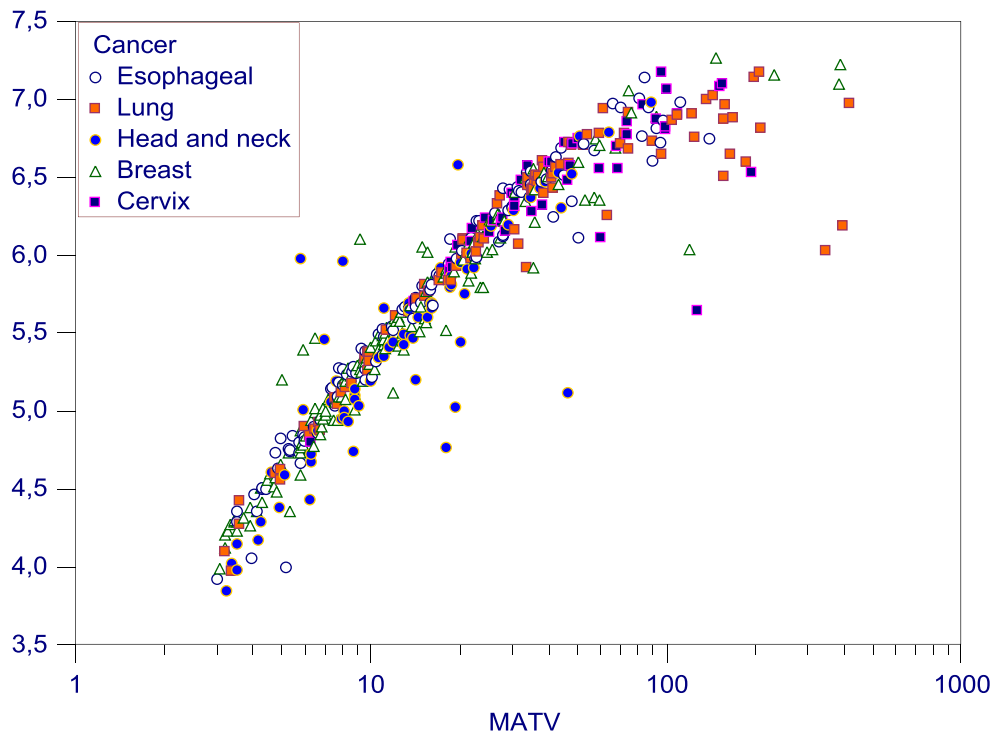
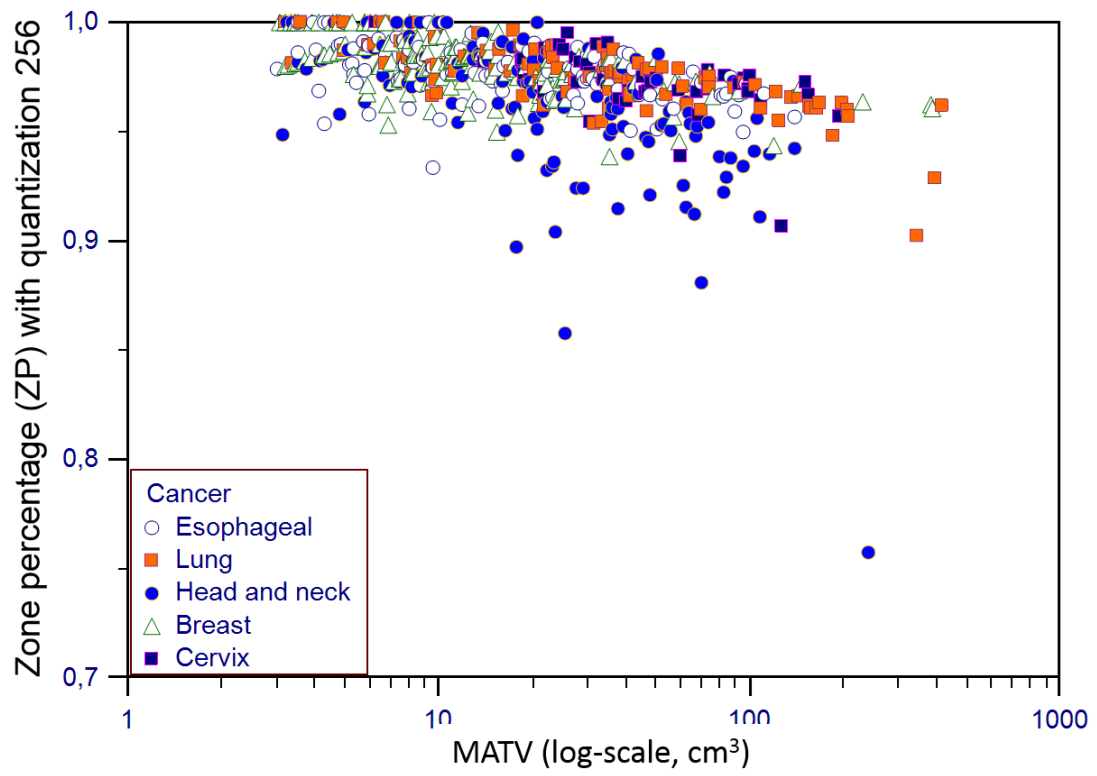
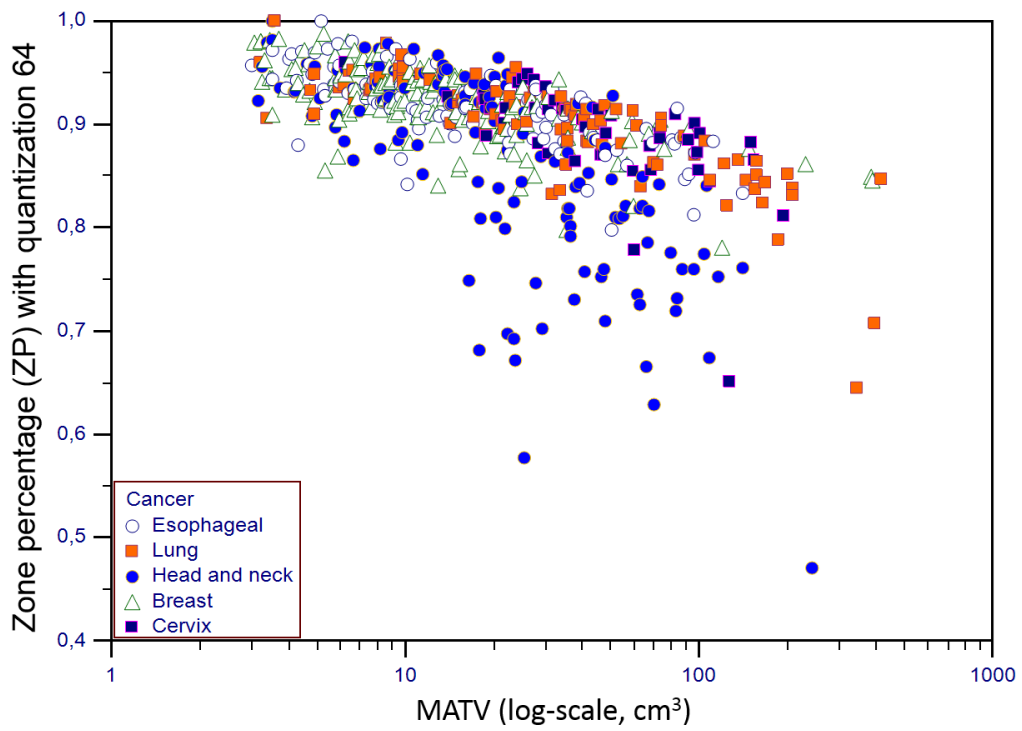


Figure 3

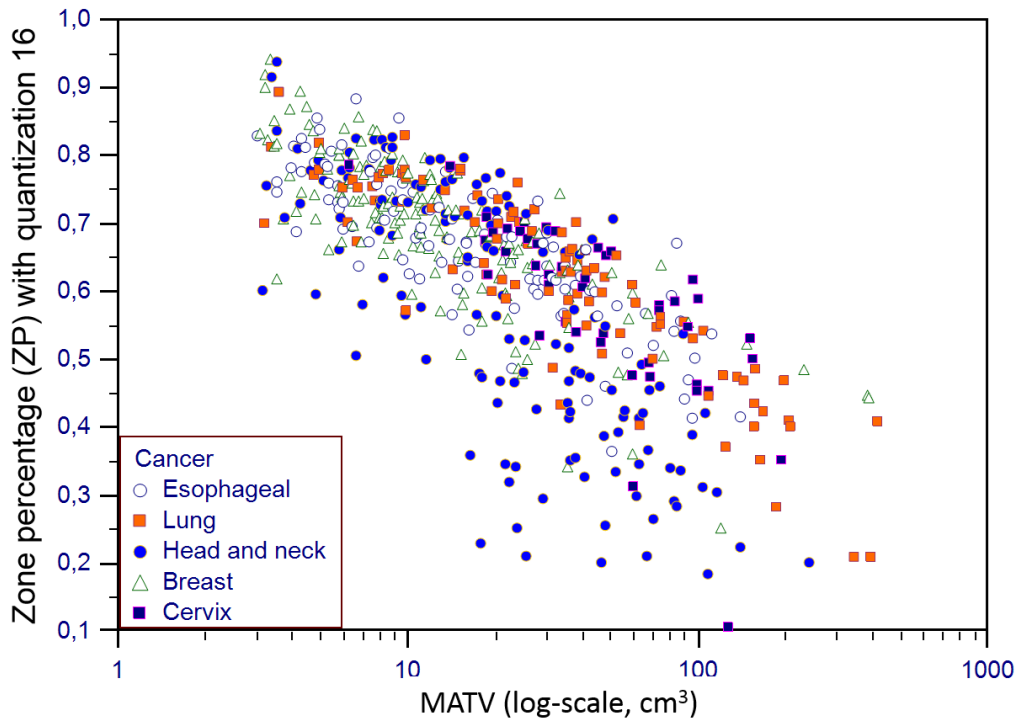
A



B



C



D

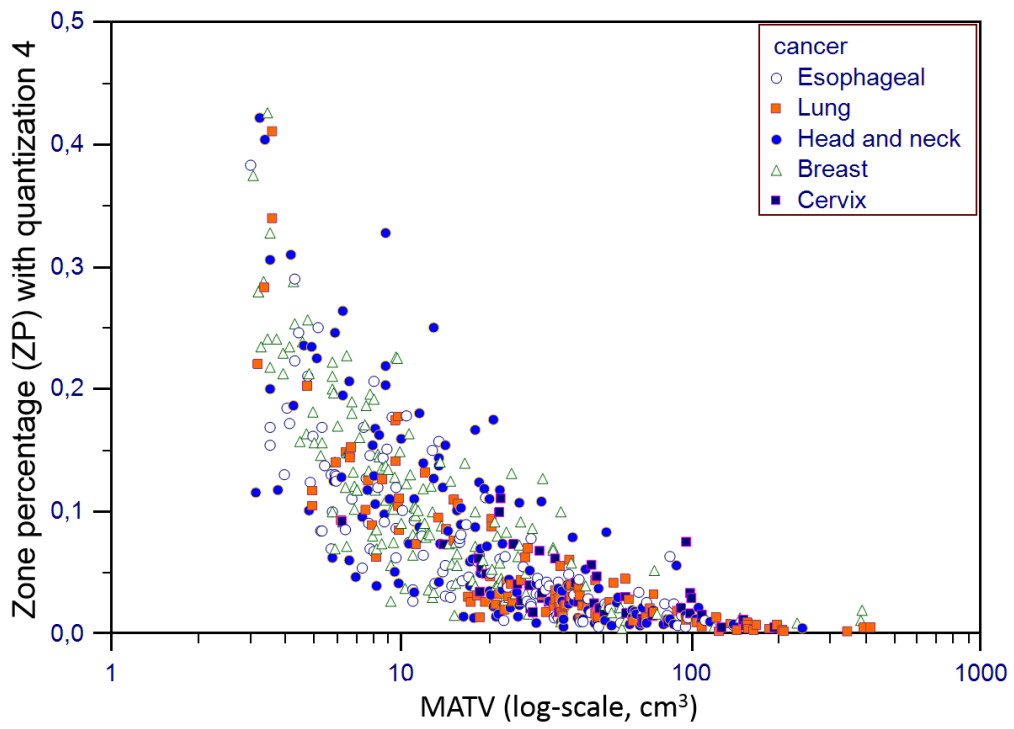
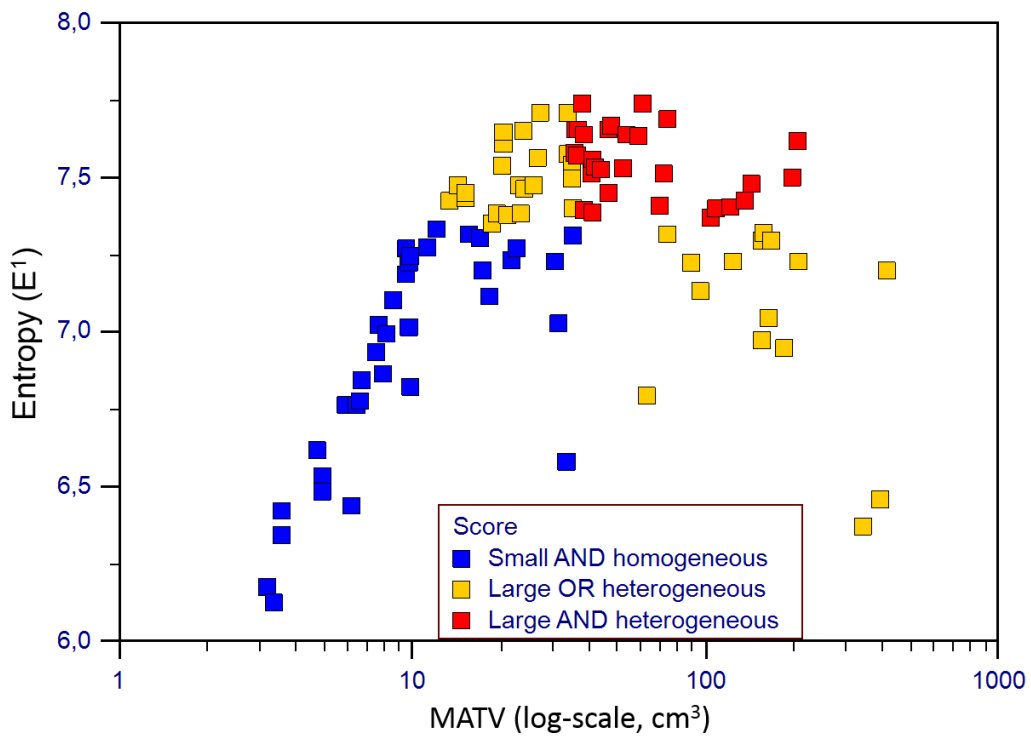


Figure 4

A



B

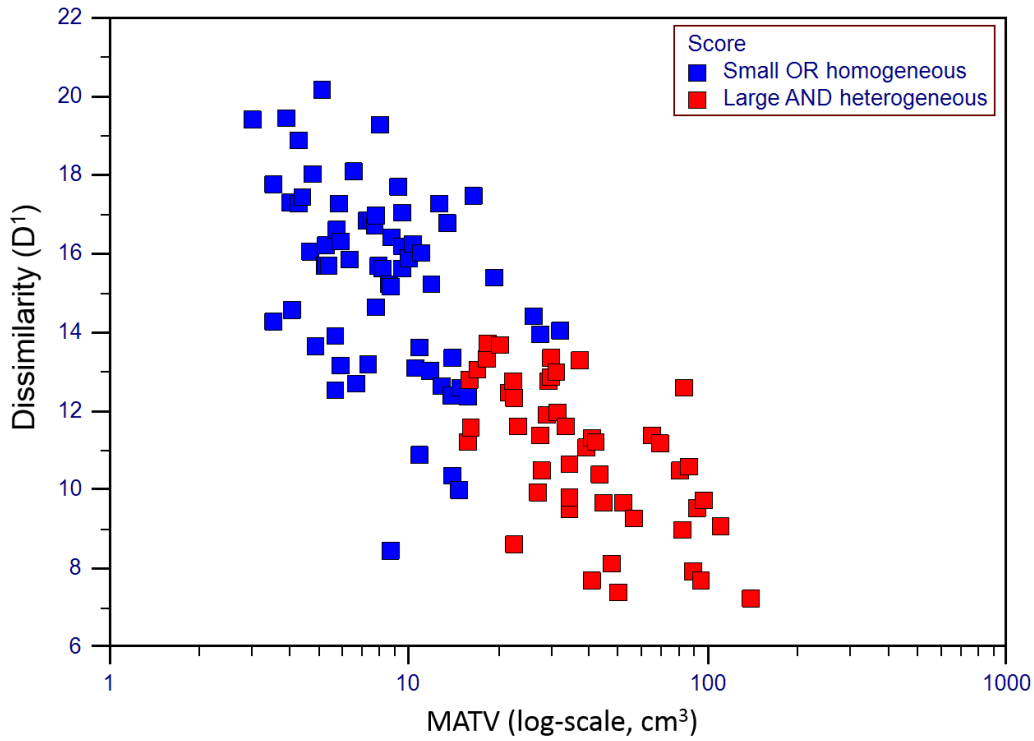


Figure 5

## Figure captions

**Figure 1:** comparison of the entropy ( $E^1$  with quantization 64) distributions with respect to MATV for each cancer site: A) esophageal, B) NSCLC, C) H&N, D) breast, E) cervix.

**Figure 2:** Distributions with respect to MATV of A) 2<sup>nd</sup> angular moment ( $ASM^1$ ) and B) homogeneity ( $H^1$ ) with quantization 64.

**Figure 3:** Distributions of entropy with respect to MATV with (A)  $E^{13}$  and quantization 256, (B)  $E^{13}$  and quantization 64.

**Figure 4:** Distributions of zone percentage with respect to MATV according to quantization (A) 256, (B) 64, (C) 16 and (D) 4.

**Figure 5:** Distributions of (A) dissimilarity ( $D^1$  with quantization=64) and (B) entropy ( $E^1$  with quantization=64) with respect to MATV with the clustering into (A) two groups and (B) three groups corresponding to survival curves of (A) figure 7A and (B) 7C.