

Supplementary Materials: Radical Hemithoracic Radiotherapy Induces Systemic Metabolomics Changes That Are Associated With The Clinical Outcome Of Malignant Pleural Mesothelioma Patients

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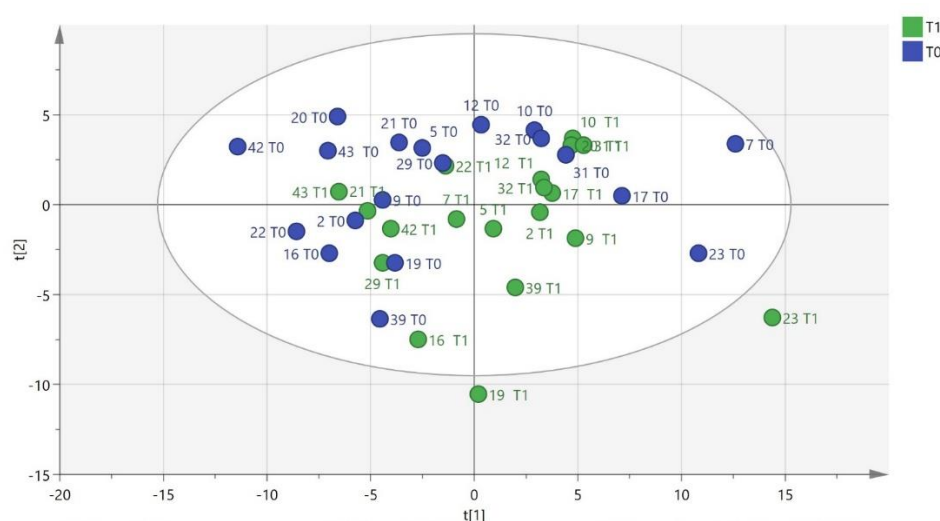


Figure S1. PCA of metabolomics profiles of 19 MPM patients before (T₀) and after (T₁) RHRT.

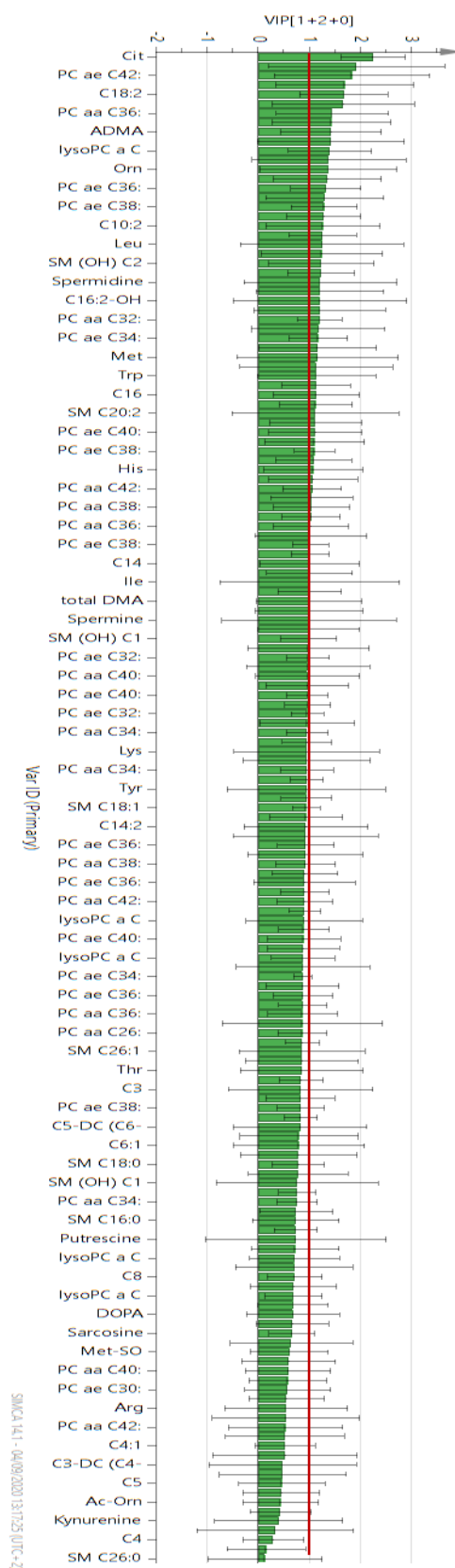


Figure S2. Metabolites ranked according to their VIP scores in the OPLS-DA model. The bars in the histograms are the confidence intervals derived from jack-knifing.

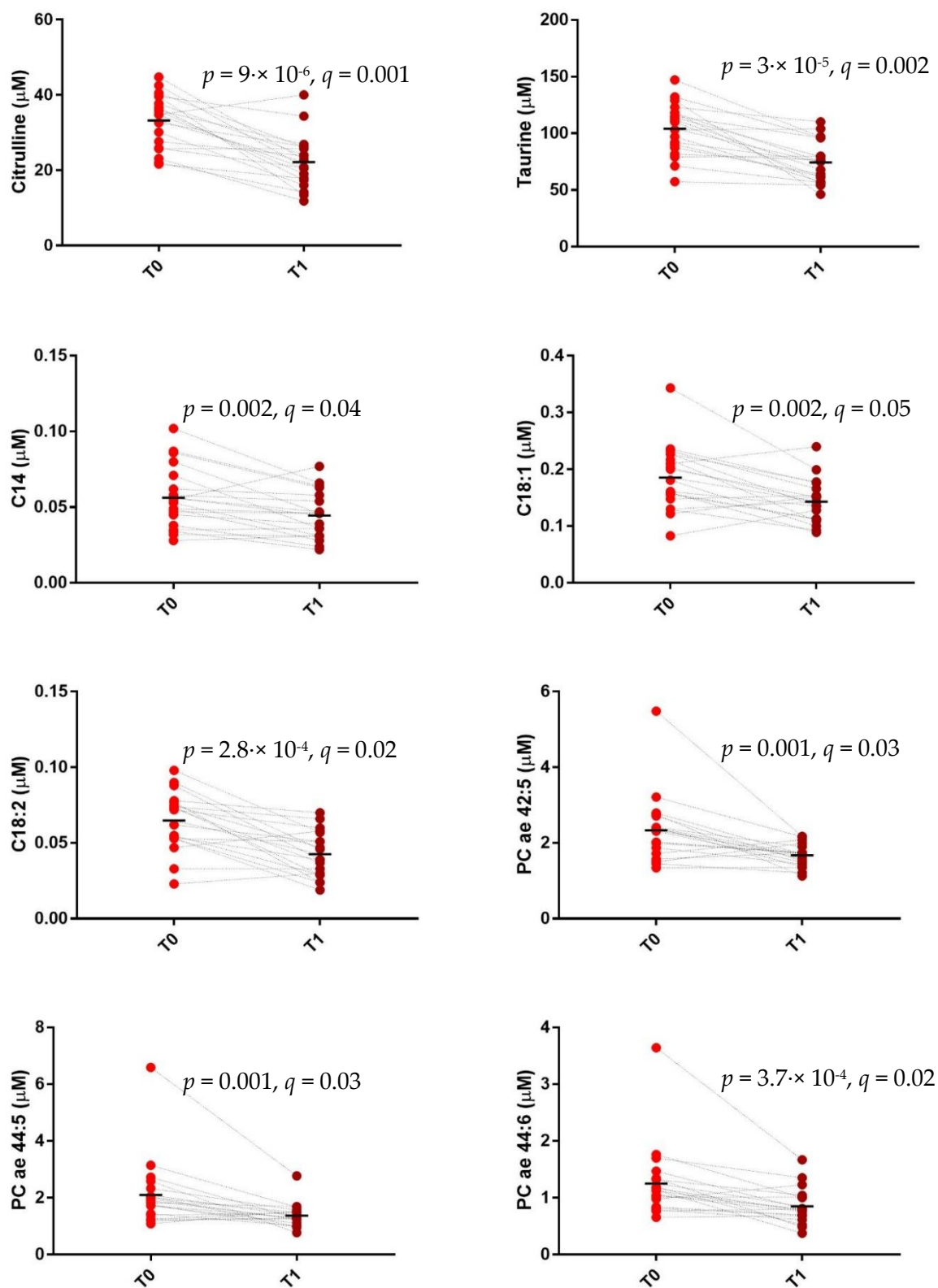


Figure S3. Serum concentrations at baseline (T₀) and post-RHRT (T₁) for metabolites resulted significantly altered ($q < 0.05$, Student's *t*-test) in each MPM patient ($n = 19$) underwent RHRT. The black line indicates the average value for both time points.

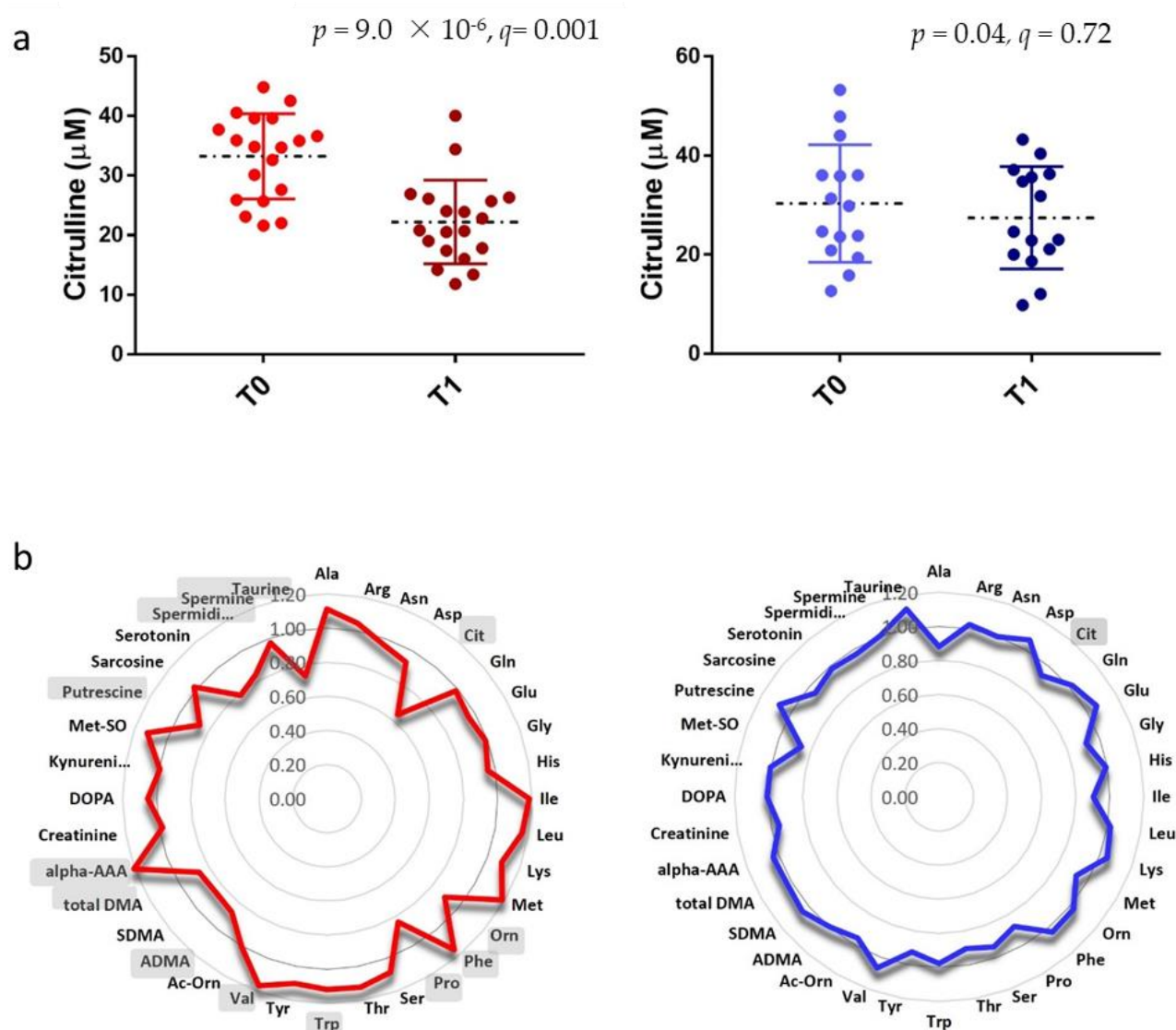


Figure S4. Citrulline serum concentrations at baseline (T0) and post-RHRT (T1) in MPM patients underwent RHRT (left) and LRT (right) (**a**). Mean fold changes of serum amino acids and derivatives in MPM patients under RHRT treatment (red, $n = 19$) and under LRT (blue, $n = 15$). Metabolites significantly changed in patients underwent RHRT are highlighted in grey (**b**).

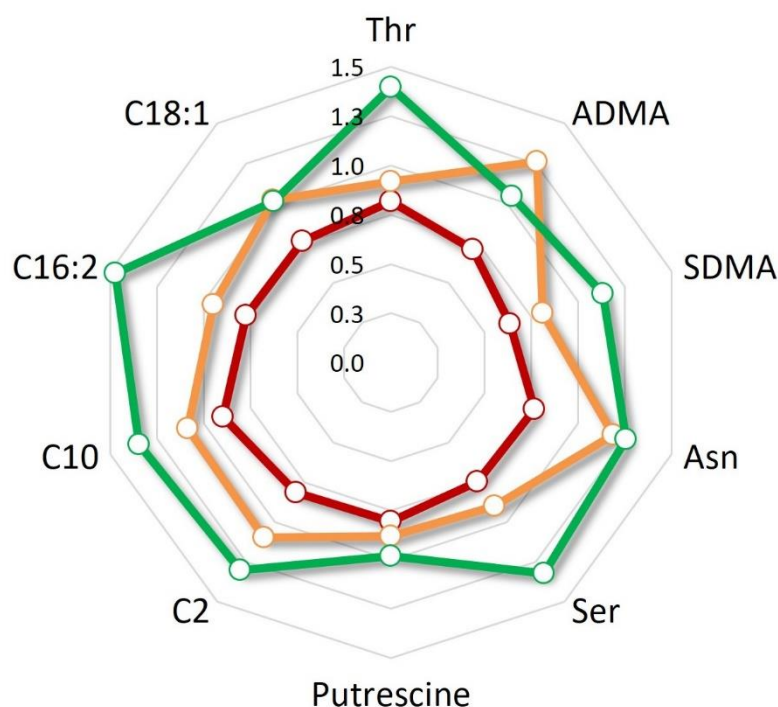


Figure S5. Mean fold change (ratio T_1/T_0) of metabolites correlated with OS in patients classified in quartiles according to OS. Short survival patients with low OS belonging to Q1 (red) had a mean fold change <1 , conversely patients of Q2 (orange) with medium OS and patients of Q4 (green) with high OS showed a mean fold change ≥ 1 ($p = 0.001$).

Table S1. Metabolites included in the targeted metabolomics analysis.

Metabolites Class	<i>n</i>	Abbreviations
Amino acids	21	Ala, Arg, Asn, Asp, Cit, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Orn, Phe, Pro, Ser, Thr, Trp, Tyr, Val.
Biogenic amines	19	ADMA, AcOrn, carnosine, creatinine, histamine, kynurenine, Met-SO, Nitro-Tyr, OHPro, PEA, Putrescine, SDMA, sarcosine, serotonin, spermidine, spermine, taurine, alphaAAA, totalDMA.
Carnitine	1	C0
Acylcarnitines	39	C2, C3, C3:1, C4, C4:1, C5, C5:1, C6 (or C4:1-DC), C6:1, C8, C8:1, C9, C10, C10:1, C10:2, C12, C12:1, C14, C14:1, C14:2, C16, C16:1, C16:2, C18, C18:1, C18:2, C3-OH, C4-OH (or C3-DC), C5-DC (or C6-OH), C5-OH (or C3-DC-M), C5:1-DC, C5-MDC, C7-DC, C12-DC, C14:1-OH, C14:2-OH, C16:1-OH, C16:2-OH, C16-OH, C18:1-OH.
Hexoses	1	H1
Sphingomyelins	15	SM 16:0, SM 16:1, SM 18:0, SM 18:1, SM 20:2, SM 22:3, SM 24:0, SM 24:1, SM 26:0, SM 26:1,

		SM (OH) 14:1, SM (OH) 16:1, SM (OH) 22:1, SM(OH) 22:2, SM (OH) 24:1.
		PC aa 24:0/26:0/28:1/30:0/30:2/32:0/32:1/32:2/32:3/3 4:1/34:2/34:3/34:4/36:0/36:1/36:2/36:3/36:4/C3 6:5/36:6/38:0/38:1/38:3/38:4/38:5/38:6/40:1/40 :2/40:3/40:4/40:5/40:6/42:0/42:1/42:2/42:4/42: 5/42:6.
Diacyl-phosphatidyl- cholines	38	
		PC ae 30:0/30:1/30:2/32:1/32:2/34:0/34:1/34:2/34:3/C 36:0/C36:1/36:2/36:3/36:4/36:5/38:0/38:1/38:2/ 38:3/38:4/38:5/38:6/40:0/40:1/40:2/40:3/40:4/4 0:5/40:6/42:0/42:1/42:2/42:3/42:4/42:5/44:3/44 :4/44:5/44:6.
Acyl-alkylphosphati- dylcholines	39	
		LysoPC aa 6:0/14:0/16:0/16:1/17:0/18:0/18:1/18:2/20:3/20 :4/24:0/26:0/26:1/28:0/28:1.
Lyso-phosphatidyl- cholines	15	

Table S2. Clinical characteristics of LRT patients' group (n=15).

Characteristics	n (%)
Age (years), median, range	74 (51–80)
Sex	
Female	0
Male	15 (100%)
Performance Status *	
0	6 (40%)
1	7 (47%)
2	2 (13%)
Histology	
Epithelioid	11 (73%)
Non-epithelioid	4 (27%)
Stage	
I-II	6 (40%)
III-IV	9 (60%)
Chemotherapy	
Pemetrexed, cisplatin	15 (100%)
Surgery	
Pleurectomy/Decortication (P/D)	4 (27%)
Decortication	1 (6%)
Biopsy	10 (67%)

* Evaluated by ECOG, Eastern Cooperative Oncology Group.