RESULTS: The overall MS was 17 months and 10.5, 11, 21, 14, 31, and 16, 5 months for patients with respectively 5, 6, 7, 8, 9, 10 and 11 to 21 BM. According histology, the MS was 25, 9 and 18 months for patients with NSCLC, melanoma with respectively breast, melanoma and lung cancer. 

CONCLUSIONS: The median survival of patients with more than 4 BM was 17 months and not influenced by histology such as breast, melanoma and lung cancer. The number of BM is not a key factor for survival in patients with otherwise good prognostic factors.

P13.14 TRANSENDOTHELIAL MIGRATION OF NON- small cancer CELLS: ROLE OF CD15 AND CD15s IN BRAIN METASTASIS
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INTRODUCTION: Metastatic non-small cell lung cancer represents the most common cause of brain metastasis in adults. Interaction between circulating cancer cells and brain endothelial cells play a key role in brain metastasis, but their underlying molecular mechanisms are still not fully understood. The CD15 and CD15s epitopes function as cell adhesion molecules and are known to be correlated with metastasis in non-CNS cancers. The aim of this study is to investigate the role of CD15 and CD15s in brain adhesion and trans-endothelial migration during metastasis to the brain by perturbing the expression of the fucosyltransferases responsible for the synthesis of these epitopes.

METHODS: The genes encoding fucosyltransferase 4 (FUT4) responsible for CD15 and fucosyltransferase 7 (FUT7) for CD15s were genetically manipulated in four human cancer cell lines: metastatic lung to brain cancer (SESTA-001), metastatic lung to lymph node (NCI-H299), primary lung carcinoma (COR-L105) and glioblastoma (UP-007) cells. Adhesion and trans-endothelial migration ability of above mentioned cells were evaluated using cell-cell adhesion assays, voltimeter (EVOM™), electric cell-substrate impedance sensing (ECIS) system and CellZscope™ respectively.

RESULTS: Both CD15 (FUT4) and CD15s (FUT7) expression were successfully manipulated in all cell lines. FUT4 induced expression resulted in an increased in adhesion of all cancer cells (p<0.01) while, FUT4 knockdown resulted in a decrease in adhesion (2 fold) compared to wild type controls (p<0.01). Similarly, FUT7 overexpression resulted in an increased the adhesion of cancer cells (2 fold) compared to wild type. Silencing of FUT7 led to a decrease in adhesion of SESTA-001 (2.5 fold), NCI-H299 (2.7 fold), COR-L105 (2.8 fold) and UP-007 (2.8 fold) compared to wild type (p<0.01). Cell lines forced to overexpress FUT4 or 7 and then added onto an endothelial monolayer caused a sharp and immediate decrease in trans-endothelial electrical resistance (TEER) values compared to knockdown and control cells (p<0.01). Knockdown of either FUT4 or 7 in metastatic cell lines lost the ability to generate a decrease in TEER compared to control cells (p<0.01).

CONCLUSIONS: This study highlights the importance of CD15 and CD15s specifically in adhesion and transendothelial migration of NSCLC cells to the brain. Targeting these carbohydrate epitopes or the fucosyltransferases responsible for their presence might contribute to reducing brain metastasis.

P13.15 MULTI-FRACTION STEREOTACTIC RADIOSURGERY (MF-SRS) VERSUS SURGERY PLUS MF-SRS FOR PATIENTS WITH LARGE RADIO RESISTANT BRAIN METASTASES (G. Minniti)1,2
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PURPOSE: Both surgery and radiosurgery (SRS) are frequently used in the initial management of patients with brain metastases. We have evaluated the local control and the radiation-induced brain necrosis in patients with large resistant brain metastases >2 cm in size treated with MF-SRS (3 x 9 Gy) or surgery plus MF-SRS for large resistant brain metastases.

METHODS: The patients consisted of 27 women and 13 men with a median age of 59 years (range 35–76) at LM. Primary cancers were lung (LC) in 24, melanoma (M) in 21 and renal cell carcinoma (RCC) in 17. The genes encoding fucosyltransferase 4 (FUT4) and fucosyltransferase 7 (FUT7) were genetically manipulated in all cell lines. Adhesion and trans-endothelial migration ability of above mentioned cells were evaluated using cell-cell adhesion assays, voltimeter (EVOM™), electric cell-substrate impedance sensing (ECIS) system and CellZscope™ respectively.

RESULTS: Both CD15 (FUT4) and CD15s (FUT7) expression were successfully manipulated in all cell lines. FUT4 induced expression resulted in an increased in adhesion of all cancer cells (p<0.01) while, FUT4 knockdown resulted in a decrease in adhesion (2 fold) compared to wild type controls (p<0.01). Similarly, FUT7 overexpression resulted in an increased the adhesion of cancer cells (2 fold) compared to wild type. Silencing of FUT7 led to a decrease in adhesion of SESTA-001 (2.5 fold), NCI-H299 (2.7 fold), COR-L105 (2.8 fold) and UP-007 (2.8 fold) compared to wild type (p<0.01). Cell lines forced to overexpress FUT4 or 7 and then added onto an endothelial monolayer caused a sharp and immediate decrease in trans-endothelial electrical resistance (TEER) values compared to knockdown and control cells (p<0.01). Knockdown of either FUT4 or 7 in metastatic cell lines lost the ability to generate a decrease in TEER compared to control cells (p<0.01).

CONCLUSIONS: This study highlights the importance of CD15 and CD15s specifically in adhesion and transendothelial migration of NSCLC cells to the brain. Targeting these carbohydrate epitopes or the fucosyltransferases responsible for their presence might contribute to reducing brain metastasis.

P13.16 CHANGES IN PERFUSION MR IMAGING IN BRAIN METASTASES AFTER STEREOTACTIC RADIOTHERAPY (M. Kerkhof)1, L. Ganne1, R. G. J. Wijgengraaf2, G. J. Lycklama à Nijehol1, S. Hammer2, M. J. B. Taphoorn2,1, L. Dirven2, M. J. Vos2
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INTRODUCTION: To assess the changes in perfusion-weighted (PWI) magnetic resonance imaging (MRI) in brain metastases after stereotactic radiotherapy (SRT), and to correlate these results with tumor response on conventional MR imaging.

METHODS: Serial MR imaging including PWI was performed on patients with brain metastases who received SRT between 2011 and 2013. These MR images were evaluated retrospectively at baseline (prior to SRT), 3 and 6 months after SRT. Size of metastases, size of surrounding edema and the relative cerebral blood volume (rCBV) were evaluated at each time point. The rCBV was assessed by subjective visual inspection of the rCBV maps in the contrast-enhanced area (visual method). The tumor responses of metastases were categorized into four groups based on changes in contrast enhancement on T1-weighted images during follow up or based on a histologically confirmed diagnosis; (1) tumor progression (TP), (2) pseudo-progression (PsPD), (3) non-progressive disease (non-PD) and (4) progression unspecified (PU). All cases showing a decrease in tumor shunting and chemo cated as non-PD. Metastases with an initial increase in size, but without a subsequent increase in size, were categorized as PU. This group could include both PaPD and TP, which could not be further specified based on (missing) follow-up. PaPD was defined as a decrease of size on T1WI after an initial increase of contrast enhancement of at least 5%. TP was based on a histological diagnosis.

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