MULTIMODAL IMAGING IN AN EXPERIMENTAL RAT MODEL FOR BRAIN METASTASIS

Valerie De Meulenaere (1), Christian Vanhove (2), Sara Neyt (3), Bert Vandeghinste (3), Pieter Mollet (3), Elke Decrock (4), Olivier De Wever (5), Benedicte Descamps (2), Karel Deblaere (1)

Department of Radiology and Nuclear Medicine, Ghent University, Ghent, Belgium, (2) IBITECH - Medisip - Infinity lab, Ghent University, Ghent, Belgium, (3) MOLECUBES NV, Ghent, Belgium, (4) Department of Basic Medical Sciences, Ghent University, Ghent, Belgium, (5) Department of Experimental Cancer Research, Ghent University, Ghent, Belgium

INTRODUCTION

Metastatic brain tumors are a severe problem in the treatment of patients with breast carcinoma. We developed a rat model for brain metastasis that allows follow-up by MRI. Injection of cancer cells labeled with iron oxide particles, allows tracking from the single-cell stage until the appearance of full-blown metastases.

RAT MODEL FOR BREAST CANCER BRAIN METASTASIS

MDA-MB-231BR/eGFP human breast cancer cells were labeled with micron-sized particles of iron oxide (MPIO; 1µm). 13 female nude rats were intracardially injected with $10^5$ labeled cells at the age of 5 weeks (Yoneda et al. J Bone Miner Res 2001, 16: 1486-1495). MRI was performed on a 7T system (PharmaScan) at day 1, and then weekly until 10 weeks post-injection, taking human endpoints into account. T2*W images were acquired one day post-injection to show the initial distribution of MPIO-labeled cells in the brain. T2W and contrast-enhanced T1W sequences were acquired to determine metastasis development outside the brain. A static whole-body $^{18}$F-FDG PET (bèta-CUBE, MOLECUBES NV, 10 MBq, 30 minutes acquisition) was performed to determine metastasis development outside the brain. For detection of bone metastases full body spiral high-resolution CT acquisitions were performed (X-CUBE, MOLECUBES NV, 7 minutes acquisition). (Fig. 1)

MRI – DETECTION OF BRAIN METASTASES

Fig. 2: In vivo serial T2W MRI scans showing metastasis as soon as three weeks post-injection. Total metastatic volume 4 weeks post-injection: 62,21 mm$^3$ ± 45 mm$^3$ – Number of metastases 4 weeks post-injection: 95 ± 60.

HIGH RESOLUTION CT AND $^{18}$F-FDG PET-CT – DETECTION OF METASTASES OUTSIDE THE BRAIN

Fig. 3: CT evaluation showed metastasis throughout the skeleton in ~80% of the rats.

Fig. 4: $^{18}$F-FDG PET-CT scan.

DISCUSSION AND CONCLUSION

Our aim was to develop a rat model for brain metastasis. However, early formation of metastases outside the brain was observed, as evidenced by CT and PET. This indicates that this model is currently not suited for investigating brain metastasis and associated treatment strategies. Therefore, the brain metastatic propensity of the cell line will be optimized by in vivo passaging.

AKNOWLEDGEMENTS

The MDA-MB-231BR/eGFP cell line was a kind gift of Dr. P. Steeg from the National Cancer Institute, Bethesda.