COMPARISON OF LIPID IMAGING IN A ZEBRAFISH MELANOMA MODEL BY POSITION EMISSION TOMOGRAPHY (PET) AND DESORPTION ELECTROSPRAY-IONIZATION-MASS SPECTROMETRY (DESI-MS)

Emrys Jones1; Fiona Henderson1; Anthony Miley2; Adam Hurst3; Duncan Foster3; Hannah Johnston3; Kaye Williams2; Michael A Batey2; Adam W McMahon3; Emmanuelle Claude1;2

1. Waters Corporation, Willows, UK; 2. Wolfson Molecular Imaging Centre, Manchester, UK; 3. Waters Corporation, Beverly, Massachusetts, US.

INTRODUCTION

Tumour heterogeneity in cancer can be a major problem for both diagnosis and therapy. Lipids are involved in membrane formation and signalling, and can be altered during cancer progression. Understanding of lipid heterogeneity is vital in elucidation of mechanisms of tumour lipid metabolism. Imaging techniques are widely used in cancer research and treatment, and techniques such as Positron Emission Tomography (PET) are used clinically to enable the visualisation of lipid metabolites in 3D. Mass Spectrometry Imaging (MSI) is an untargeted technique which does not require radio labelled tracers and can provide a wealth of molecular information. In the work described here, we compare the use of a radioactive 18F Fluoro-6-hexadecenoic acid (18F-FTHA) tracer administered to zebrafish and imaged by PET, to an imaging stable FTHA imaging experiment using Direct Environmental Spray Ionization (DESI) Mass Spectrometry.

METHODS

Zebrafish sample preparation

The lipoprotein lipase mutant and wild type zebrafish used for the PET experiment were immersed for 30 min in 100 mL of water containing 60Mg (~0.5 ppm) of [18F] fluoro-6-hexadecenoic acid (FTHA) tracer (figure 1). The wild type zebrafish used for the DESI imaging experiment were immersed for 30 min in 100 mL water containing 0.5 mg of [18F]-fluoro-6-hexadecenoic acid (FTHA) tracer. Fish were then placed in cuvettes (held in place with sponge) and cuvettes placed in falcin tubes filled with ice to maintain anaesthesia.

PET Imaging

Static PET scans were then performed for 5 and 10 minutes on a pre-clinical PET scanner (Inveon, Siemens, Germany).

Tissue sections

The tumour bearing zebrafish was culled immediately after PET scanning, and flash-frozen in isopentane. 12 μm thick sections of both zebrafish were produced using a cryotome onto standard glass slides.

Mass spectrometry imaging

The principle of DESI imaging is shown in figure 2. DESI uses an electrospray to desorb ions from the surface of a sample, which are directed into a mass spectrometer for analysis. This technique allows both spatial localization and discrimination of metabolites determined. Experiments were carried out using a modified 2D DESI stage mounted on a Waters Xevo-G2-QS mass spectrometer (figure 2). DESI spray conditions were set at 2 μl/min, 95:5 methanol:water with a nebulising gas pressure of 4 bar. Data was analysed using High Definition Imaging (HDI) software.

RESULTS

PET experiments were carried out using [18F] FTHA, which is a palmitic acid analogue used to visualise lipid metabolism in tumours. As shown in figure 3, A), the PET scan of the wild type zebrafish shows that FTHA tracer was uptake mainly in the gut part of the animal, with some uptake in the tail and the head. The uptake of the tracer in the tumour bearing bearing zebrafish shows a similar profile throughout the animal with some tracer in the tumour region. Furthermore the uptake of the tracer within the tumour looks homogenous within the spatial resolution of the PET scan.

With DESI imaging, the FTHA tracer was only observed within the zebrafish in area of high concentration. [18F]FTHA tracer was also localised in the wild type zebrafish mainly in the gut, tail and head of the animal (see figure 4). However the [18F]FTHA tracer was not detected in the tumour bearing zebrafish, presumably due to lack of contrast and for the positive and negative DESI imaging datasets.

In figure 5A), it can be observed that the lipid signal is enhanced on average by a factor of 3 to 4 in the tumour region. In figure 6A) it can be observed that the lipid signal is significantly enhanced in the tumour region compared to the non-tumour region of the same zebrafish.

CONCLUSIONS

PET and DESI imaging techniques produce complementary information.

• By DESI imaging, the tracer was only observed in the wild type zebrafish ([18F]FTHA tracer) and not in the tumour bearing zebrafish ([18F]FTHA tracer).

• PET imaging showed homogenous uptake of the FTHA tracer into the tumour region of the lipoprotein lipase mutant zebrafish with poor spatial resolution.

• However, DESI imaging gave rich molecular ion information from lipids and metabolites, and showed tumour heterogeneity, with visualization of lipid localization which could be important for disease analysis.

References:

©2015 Waters Corporation