MRI with hyperpolarised [1-13C]pyruvate detects advanced pancreatic preneoplasia prior to invasive disease in a mouse model.

Pancreatic cancer (PCa) is treatable by surgery when detected at an early stage. Non-invasive imaging methods able to detect both established tumours and their precursor lesions are needed to select patients for surgery. We investigated here whether pancreatic preneoplasia could be detected prior to the development of invasive cancers in genetically engineered mouse models of PCa using metabolic imaging. The concentrations of alanine and lactate and the activities of lactate dehydrogenase (LDH) and alanine aminotransferase (ALT) were measured in extracts prepared from the pancreas of animals at different stages of disease progression; from pancreatitis, through tissue with predominantly low-grade and then high-grade pancreatic intraepithelial neoplasia and then tumour. (13)C magnetic resonance spectroscopic imaging ((13)C-MRSI) was used to measure non-invasively changes in (13)C labelling of alanine and lactate with disease progression, following injection of hyperpolarised [1-(13)C]pyruvate. Progressive decreases in the alanine/lactate concentration ratio and ALT/LDH activity ratio with disease progression were accompanied by a corresponding decrease in the
[1-(13)C]alanine/[1-(13)C]lactate signal ratio observed in (13)C-MRSI images of the pancreas. Metabolic imaging with hyperpolarised [1-(13)C]pyruvate enables detection and monitoring of the progression of PCa precursor lesions. Translation of this MRI technique to the clinic has the potential to improve the management of patients at high risk of developing PCa.