PROSTATE CANCER

Piloting hyperpolarized ^{13}C-pyruvate MRI for imaging advanced prostate cancer

> High k_{PL} regions on hyperpolarized ^{13}C-pyruvate MRI corresponded with radiographical evidence of metastatic disease on CT and MRI

The results of a pilot clinical study investigating the feasibility of using hyperpolarized ^{13}C-pyruvate MRI to image prostate cancer bone and/or visceral metastases in real time to assess metabolism and response to therapy have been published in *Prostate Cancer and Prostatic Diseases*.

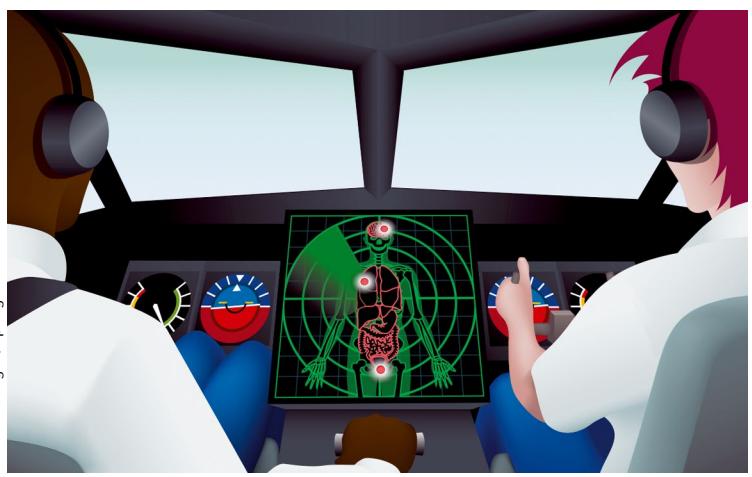
Hyperpolarized ^{13}C-pyruvate MRI is an imaging technique that is used to measure pyruvate-to-lactate metabolism, which is mediated by upregulation of lactate dehydrogenase activity in tumours caused by the Warburg effect. Characteristics of aggressive cancer include high glycolytic activity and rapid conversion of pyruvate to lactate. To date, ^{13}C-pyruvate MRI has been used successfully in localized prostate cancer to detect metabolic responses to chemohormonaltherapy.

In the current pilot study, the researchers sought to widen the use of hyperpolarized ^{13}C-pyruvate MRI by assessing its feasibility and performance in metastatic prostate cancer. In total, six patients with metastatic castration-resistant prostate cancer (mCRPC) were recruited to the study. All participants underwent restaging CT and bone scans before enrolment and had at least one lesion identified as amenable to hyperpolarized ^{13}C-pyruvate MRI. At baseline and follow-up monitoring, patients received an injection of 250 mM hyperpolarized ^{13}C-pyruvate and then imaging was conducted using clinical 3 T MRI. The rate of conversion of pyruvate to lactate (k_{PL}) from target lesions in each patient was then calculated.

At baseline imaging, high k_{PL} was observed in bone and liver metastases (mean k_{PL} $0.020 \pm 0.006\ s^{-1}$ for bone metastases and $0.026 \pm 0.000\ s^{-1}$ for liver metastases). High k_{PL} regions on hyperpolarized ^{13}C-pyruvate MRI corresponded with radiographical evidence of metastatic disease on CT and MRI. Paired CT-guided biopsy samples were available for five patients and histological examination showed evidence of metastasis. In four of five patients, histological analysis showed poorly differentiated adenocarcinoma. Discrete regions of adenocarcinoma and treatment-emergent small-cell neuroendocrine differentiation were observed in one patient. RNA sequencing of the biopsy samples revealed increased expression of *LDHA* compared with expression of the dominant isoform of *PDHA1* (log expression: 15.7 ± 0.7 versus 12.8 ± 0.9). These observations were consistent with the increased aerobic glycolysis found in the rate of pyruvate-to-lactate conversion seen using hyperpolarized ^{13}C-pyruvate MRI.

As a case study, patient 2 (who had mCRPC, liver metastasis and a low serum PSA level) initiated carboplatin plus docetaxel 24 days after having baseline hyperpolarized ^{13}C-pyruvate MRI. At the follow-up MRI, which was 62 days after the start of treatment, the conversion rate of pyruvate to lactate in the target liver metastasis had decreased from $0.026\ s^{-1}$ to $0.015\ s^{-1}$. The size of the liver lesion had also decreased by 39% (from 19.3 mm to 11.8 mm). Furthermore, PSA levels reduced by >50%.

The results of this first study to assess the use of hyperpolarized ^{13}C-pyruvate MRI for imaging prostate cancer metastases show that detecting the metabolic activity of metastases in real time is feasible and safe. This imaging modality can also be used to assess response to treatment. High k_{PL} regions showed good correlation with findings of advanced prostate cancer on biopsy. Thus, hyperpolarized ^{13}C-pyruvate MRI should be further developed and assessed for this purpose in a large, prospective study.



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ORIGINAL ARTICLE Chen, H.-Y. et al. Hyperpolarized ^{13}C-pyruvate MRI detects real-time metabolic flux in prostate cancer metastases to bone and liver: a clinical feasibility study. *Prostate Cancer Prostatic Dis.* https://doi.org/10.1038/s41391-019-0180-z (2019)