**SUPPLEMENTARY METHODS**

***Xenograft DCE-MRI acquisition details***

For DCE-MRI, native tissue VFA SPGR *R*1 calculation was performed (TR = 6.02 ms; TE = 1.46 ms; α = 2°/5°/10°), followed by 96 dynamic *T*1-weighted SPGR acquisitions (TR = 6.02 ms; TE = 1.46 ms; α = 10°; temporal resolution: 5.8 s) with gadolinium-based contrast agent (Gd-DOTA (Dotarem, Guerbet) injected into a tail vein after 24 acquisitions.

***Xenograft pathology analysis details***

Intraperitoneal injection of 60 mg/ kg pimonidazole (Hypoxyprobe, Hypoxyprobe Inc., Burlington, MA) was performed approximately 55 min before 100% oxygen inhalation began to allow for maximal bioreduction of pimonidazole in hypoxic tumor regions. Tumors were excised whole and bisected along the coronal imaging plane, allowing the cut surface to match the MRI ROI. 8 µm tissue sections were obtained from formalin fixed and paraffin embedded tumor material and scanned using fluorescent microscopy on a Panoramic 250 Flash system (3DHistech Ltd., Budapest, Hungary) to determine pimonidazole binding. Data were analyzed using Definiens Developer 2.7 Tissue Studio software (Definiens, Munich, Germany). Hypoxic fraction was represented by the percentage of stained area in viable tumor.

***Xenograft oxygen consumption rate (OCR) analysis details***

Specimens were harvested and placed directly in a tube containing ice cold mM D-Glucose, 2 mM L-Glutamine, 1 mM Sodium Pyruvate, 2 mM Sodium Citrate, pH7.4. Each sample was attached onto moulds using cyanoacrylate adhesives (Sigma, Cat# Z105899) and stabilized to the base of a Vibrotome Series 1000 Sectioning System. Once fixed to the base plate, the specimen was covered in ice cold Krebs-Henseleit buffer. Settings used to cut slices were thickness – 500 µm, amplitude – 3 mm, speed – 0.07 mm/ s. Slices were then placed into a Krebs-Henseleit buffer supplemented with 12 petri dishes on ice-containing buffer. Six biopsies were obtained per slice using 1 mm sterile disposable biopsy punch (kai Europe GmbH).

Seahorse XFe96 Spheroid Microplate was coated with Corning® Cell-TakTM cell adhesive (3.5 µg/cm2 of surface area, Cat# 354240) by overnight incubation at 40C and brought to room temperature while biopsies were prepared. Samples were transferred into the Seahorse XFe96 Spheroid Microplate containing 160 µl Seahorse XF base media (#102353-100) supplemented with 10 mM D-Glucose, 1mM sodium pyruvate and 2 mM L-glutamine. Real-time metabolic measurements for basal oxygen consumption rate (OCR) were then performed that sensed oxygen presence or absence, according to manufacturer’s protocol using an Agilent Seahorse XFe96 Analyser (Agilent Technologies). Following measurements, any individual samples with less than -5 pmol/ min values were excluded (for possible technical failure). Data are presented as OCR (pmol/min per normalized unit).

***NSCLC patient data: DCE-MRI acquisition details***

For DCE-MRI, data were acquired using a coronal 3D baseline SPGR VFA *R*1 measurement followed by a series of spoiled gradient echo measurements (TR: 3.3 ms; TE: 1.43 ms; α = 2°/4°/7°/10°) with a 10° dynamic acquisition over 75 time points (temporal resolution: 4.9 s). A bolus of 0.05 mmol/ kg gadoterate meglumine (Dotarem®, Guerbet, Aulnay-sous-Bois, France) at 1.5 ml/ s followed by an equal volume of saline were injected intravenously into a forearm vein using a Spectris MR (Medrad Inc, Indianola, PA, USA) power injector after 6 baseline measurements.

***NSCLC patient data: OE-MRI and DCE-MRI data registration***

Non-linear diffeomorphic image registration (stnava.github.io/ANTs) was applied to correct for breathing and patient motion during each of the dynamic OE-MRI and DCE-MRI acquisitions, creating motion-corrected datasets (**supplementary video 1B**). Tumor ROIs were then transferred to dynamic acquisitions and checked for spatial accuracy to ensure that the ROIs lie inside the tumor.

The motion-corrected OE-MRI dynamic series were registered to the motion-corrected DCE-MRI dynamic series for each patient visit (and for each tumor, if more than one) using linear rigid body registration (FLIRT, FSL version 5, [fsl.fmrib.ox.ac.uk/fsl/fslwiki/FLIRT](https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FLIRT)). FLIRT was applied to time-averaged baseline motion-corrected OE-MRI and motion-corrected DCE-MRI volumes, with tumor ROIs (enlarged by between 5 and 11 voxels) used to restrict the registration to the tumors. The registration process was then applied to each individual motion-corrected OE-MRI acquisition in the dynamic series.

***Legend for the supplementary video***

**Supplementary video 1 shows:** (**A**) Typical pre-processed OE-MRI and DCE-MRI dynamic acquisition showing a loop of the same slice through the 96 (OE-MRI)/ 75 (DCE-MRI) acquisition time points. (**B**) Typical OE-MRI dynamic acquisition showing a loop of the same slice through the 96 acquisition time points before and after motion correction, which was applied to correct for breathing and patient motion during dynamic OE-MRI and DCE-MRI acquisitions, creating motion-corrected datasets.