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Supplementary Materials for

Targeting brain metastases with ultrasmall theranostic nanoparticles, a first-in-human trial from an MRI perspective

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Supplementary Materials

Supplementary materials and methods

The main sequence parameters for i) the 3D T_1-weighted gradient echo sequence and ii) the 3D FLASH sequence with multiple flip angles are the following:

3D T_1-weighted gradient echo sequence: TR/TE=8.3 / 3.8ms, Flip Angle=8°, Field-of-view=256x256x220mm^3, Acquisition matrix=256x256x220, Resolution=1x1x1mm^3, duration=4min39s

3D FLASH sequence with multiple flip angles: TR/TE=8.1 / 3.8 ms, field-of-view=240x224x220mm^3, Flip Angle=5°, Acquisition matrix=240x224, Resolution=1x1x2mm^3, duration 2min51s. (repeated for Flip Angle=15, 20, and 35°)

The T_1 maps were obtained by fitting, pixel by pixel, the inversion recovery data with a 3-parameter, exponential recovery, model. The concentration of Gd^{3+} was calculated using the relaxation time determined on the T_1 maps, according to the formula $\boldsymbol{C = \frac{1}{r_1}(\frac{1}{T_{1post}} - \frac{1}{T_{1pre}})}$,

where T_{1pre} is the relaxation time before AGuIX injection (in seconds), T_{1post} is the relaxation time after nanoparticles injection (in seconds) and r_1 is the relaxivity (8.9 $mM^{-1}.s^{-1}$) per Gd^{3+} in AGuIX nanoparticle at 3 Tesla.

The MRI enhancement SE (for Signal Enhancement) was defined as $SE = (S_{post}-S_{pre})/S_{pre}$, where S_{post} and S_{pre} correspond to the MRI signal amplitude measured post and pre administration of AGuIX nanoparticles using the 3D T_1-weighted imaging sequence.

Supplementary figures

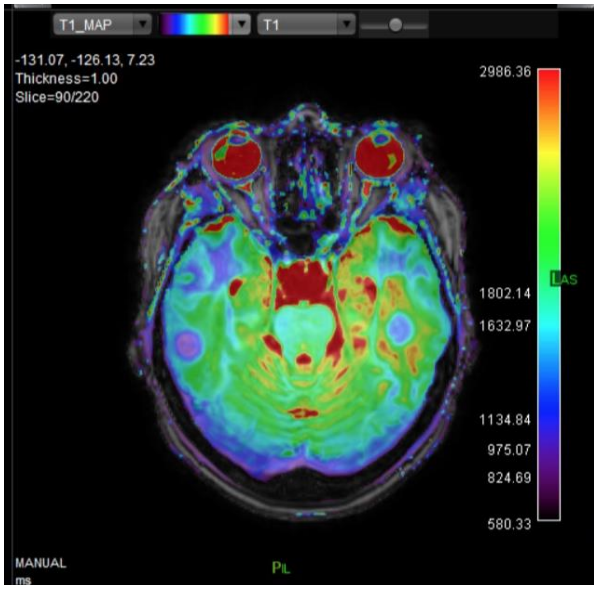

Fig. S1. **T_1 map following the injection of AGuIX nanoparticles.** This map corresponds to the image obtained in the patient with multiple NSCLC metastases shown in Figure 2. The uptake of the AGuIX nanoparticles into the two metastases results in decreased T_1 values in the tumor.