Simultaneous PET/MRI imaging using nanoparticles

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Dual Modality PET/MR Probes

• In the ideal application, dual imaging takes advantage of the best features of both modalities and compensates for the weaknesses.

• Using radiolabeled nanoparticles in combination with magnetic resonance spectroscopy and radiotracers that probe a specific function can elucidate the impact of these drugs in specific organs.

• We have combined Fe-52 core labeled and C-11 surface labeled functionalized nanoparticles to probe biodistribution and uptake kinetics.
Radiolabeled Nanoparticles

Biodistribution

Mertig et al. (2002)

[11C]CdSe/ZnS

SiO2

MINO

Organic shell modification

Core material functionalization

core size

2 nm 10 nm 20 nm

[11C]Nanoparticles

PET

Biodistribution

Metabolic Response

Biochemical Response

Microscopy

Tissue nanoparticle localization

Cell viability

Proteome analysis, biotargeted nanoprobes

18FDG nanoparticles

Metabolic response

Levels of gene expression

Mertig et al. (2002)
CHARACTERISTICS OF PET SYSTEM

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scintillator type</td>
<td>LSO (4 x 8 array)</td>
</tr>
<tr>
<td>Scintillator dimensions (mm³)</td>
<td>2.2 x 2.2 x 5</td>
</tr>
<tr>
<td>Photodetector</td>
<td>APD (4 x 8 array)</td>
</tr>
<tr>
<td>Inner diameter (mm)</td>
<td>38</td>
</tr>
<tr>
<td>Outer diameter (mm)</td>
<td>80</td>
</tr>
<tr>
<td>Transaxial FOV (mm)</td>
<td>32</td>
</tr>
<tr>
<td>Axial FOV (mm)</td>
<td>19</td>
</tr>
<tr>
<td>Spatial Resolution at cFOV (mm)</td>
<td>1.2</td>
</tr>
<tr>
<td>Energy Resolution (%)</td>
<td>14</td>
</tr>
<tr>
<td>Time Resolution (ns)</td>
<td>10</td>
</tr>
<tr>
<td>Coincidence time window (ns)</td>
<td>18</td>
</tr>
<tr>
<td>Absolute Sensitivity (%)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

PET detector with MRI coil

Animal handling platform

To the data acquisition computer and power supplies outside the MRI room

Signal processing module

Fiber optic control and data signals

Shielded multi-conductor power cables

Tuning rods
Nanoparticle Labels

100 nm diameter

Iron-52 core labeled nanoparticle

30 nm diameter

Carbon-11 surface labeled nanoparticles

0.1 mg nanoparticles injected
50 microCuries per injection
Fluorine-18 labeled nanoparticles

When we injected F-18 labeled nanoparticles, the F-18 label immediately came off and went to bone.
Precipitation of C-11 labeled Iron oxide nanoparticles

The particle settling data plotted in k show an exponential fit. j and l are digital pictures taken near to the start and end of the PET scanning, respectively. The carbon-11 label follows the same kinetics as the nanoparticles in the PET images, indicating robust labeling of nanoparticles.
Nanoparticle phantom

MRI image of iron oxide nanoparticles of different concentrations. This shows that the relative concentrations of the nanoparticles can be determined by MR imaging. It is also possible to see some clumping of the nanoparticles in the tubes. In these pictures, the lighter colors are lower concentrations and the darker disks are the higher concentrations.
Time sequence of FeO nanoparticles in mouse

The darker color in the images shows an increase in the concentration of nanoparticles in the liver.
Simultaneous PET and MRI iron oxide nanoparticles

Iron-52 labeled nanoparticles

RARE - Rapid Acquisition with Refocused Echoes
FLASH - Fast Low Angle SHot
FLASH/RARE
Pixel size = 0.15 mm
FOV = 38.4 mm
Slice thickness = 0.9 mm
Slice separation = 1 mm
Kinetics of Nanoparticle Uptake in Rat

Kinetics of Fe-52 iron labeled nanoparticle with PET and MRI taken simultaneously show the same kinetics.

Images show Fe-52 labeled iron oxide nanoparticles at 1 hour after injection (left) and at 3 days after injection (right). The distribution shows that most of the nanoparticles remain in the liver over this time period.
Liver uptake of [\textsuperscript{11}C]nanoparticles in mouse

Mouse A before [\textsuperscript{11}C]nanoparticle injection

Mouse B – control - no nanoparticle injection

Mouse A immediately after [\textsuperscript{11}C]nanoparticle injection

Mouse A - 2 days after [\textsuperscript{11}C]nanoparticle injection
Introduction of Nanoparticles

Upper left corner is mouse liver before injection of nanoparticles. Second panel shows immediate accumulation in the liver and notice the blood signal decrease due to nanoparticles in the blood.
Coregistered Simultaneous Images

\(^{11}\text{C} \) labeled nanoparticles images. The label remains intact and the PET and MRI images show the same biodistribution.
Kinetics of $[^{11}\text{C}]$nanoparticles

![Graph showing the kinetics of $[^{11}\text{C}]$nanoparticles in the liver. The x-axis represents time in minutes (0-25), and the y-axis represents the acticity concentration (arb units) ranging from 0 to 0.01. The graph shows a gradual decrease in activity concentration over time, with a slight trend towards stabilization.]
2 days after nanoparticle administration

2 days after injection: Here are some more images from today's rescan of the mouse we injected with FeO on Monday (except for the upper left hand image). The upper left hand image is the control mouse from yesterday, the upper middle image was taken on Monday post injection and all of the rest were acquired today during the rescan on the injected mouse. We plan to repeat this in two weeks and perhaps periodically thereafter.
The attached panel of images compares similar views of the nanoparticle injected mouse A (1st and 3rd rows) to the uninjected mouse B that we scanned previously (2nd and 4th rows). Clearly, the FeO remains in the liver. However, images comparing the kidneys and livers of the two animals (3rd from left in rows 3 and 4) using a T2 weighted imaging sequence, appears to show subtle changes in the kidney of the nanoparticle injected mouse. Comparisons of the brains appear similar.
Example: Multiscale analysis of exposure

**Biodistribution**

[¹¹C]Nanoparticles

- **Core material functionalization**
  - 2 nm
  - 10 nm
  - 20 nm

**Microscopy**

- Tissue nanoparticle localization
- Cell viability

**PET**

- Biodistribution
- Metabolic response
- Biochemical response

**Proteome analysis, bio-targeted nanoprobes**

- Levels of gene expression

**18FDG nanoparticles**

- Metabolic response

Mertig et al. (2002)
Simultaneous PET/MRI of the rat brain in 9.4 T with MRS

FLASH Gradient Echo

RARE Spin Echo

MRS – PET ON

ppm
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Size-dependent kinetics of $^{11}$C-CdSe/ZnS

Lines depict the fit of each time activity curve to a two compartment model using a region of interest over the heart as input.