"Why & Now"
Intro to PET and PET/MRI

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### All 6(!) FDA-Approved PET Imaging Agents

<table>
<thead>
<tr>
<th>AMMONIA N 13</th>
<th>AMMONIA, N-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMYVID</td>
<td>FLORBETAPIR F-18</td>
</tr>
<tr>
<td>CARDIOGEN-82</td>
<td>RUBIDIIUM CHLORIDE RB-82</td>
</tr>
<tr>
<td>CHOLINE C-11</td>
<td>CHOLINE C-11</td>
</tr>
<tr>
<td>FLUDEOXYGLUCOSE F 18</td>
<td>FLUDEOXYGLUCOSE F-18</td>
</tr>
<tr>
<td>VIZAMYL</td>
<td>FLUMETAMOL F-18</td>
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</table>

- Only **6** PET radiotracers have been approved by the FDA for a diagnostic indication.
- Only **1** PET radiotracer is used routinely in clinical practice.
- Most PET radiotracers are used in clinical and preclinical research. We’ll focus on concepts that will be helpful for you as you think about developing a PET radiotracer for a new application.
2-deoxy-2-(^18F)fluoro-D-glucose
Fluorodeoxyglucose (^18F) or fludeoxyglucose (^18F)

[^18F]FDG

[^18F]FDG is indicated in positron emission tomography (PET) imaging for (1) assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer; (2) patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging, for the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function; and (3) patients for the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.
$^{18}$FDG essentially is PET

Distribution Network of FDG - 2005
Choline is an essential nutrient we get from diet. Used in phospholipid synthesis (cell membranes) and in the brain (acetylcholine, neurotransmitter).

\(^{11}\text{C}\)Choline incorporates into tumor cells through an active, carrier-mediated transport mechanism for choline. It is phosphorylated intracellularly by choline kinase, an enzyme frequently upregulated in human tumors, yielding phosphoryl \(^{11}\text{C}\)choline, which is integrated into phospholipids in the cell membrane as part of phosphatidylcholine.

Choline C 11 Injection is approved for patients with suspected prostate cancer recurrence and non-informative bone scintigraphy, computerized tomography (CT) or magnetic resonance imaging.
[\textsubscript{\textsuperscript{13}}N]Ammonia & [\textsuperscript{82}Rb]Rubidium

Ammonia N 13 Injection AND Rubidium Rb 82 chloride injection are indicated for diagnostic PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

\begin{itemize}
  \item N-13 \hspace{1em} \text{Half-Life} = 9.98 \text{ min}
  \item Rb-82 \hspace{1em} \text{Half-Life} = 1.27 \text{ min}
\end{itemize}
FLORBETAPIR F-18

[^{18F}]Amyvid

Cognitively Normal

Aβ- MCI

Aβ+ AD

Aβ+ MCI
Initial U.S. Approval: 2012

--------------------------------- INDICATIONS AND USAGE ---------------------------------

Amyvid is a radioactive diagnostic agent for Positron Emission Tomography (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer’s Disease (AD) and other causes of cognitive decline. A negative Amyvid scan indicates sparse to no neuritic plaques, and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient’s cognitive impairment is due to AD. A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations (1).

Limitations of Use

- A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder (1).
- Safety and effectiveness of Amyvid have not been established for:
  - Predicting development of dementia or other neurologic condition;
  - Monitoring responses to therapies (1).
Key Features of Imaging with PET

- Isotopic substitution (for example with carbon-11): Direct Observation of target molecule

- High Sensitivity \((10^{-11}-10^{-12} \text{ M})\): Only nanograms to low micrograms of molecular probe used!

- Ability to rapidly translate to Humans

- Imaging is quantitative with and allows for direct interpretation

Adapted from:

High Specific Activity = Low Mass
Types of information that PET can provide

Pharmacokinetics

Information about a radiolabeled drug

PK/PD

Molecular-level information about a biological event

Radiotracers are unique in that they exhibit **saturable binding** (also known as specific binding)
1. **Isotope Production**

   - Proton beam (11 MeV) is accelerated in a cyclotron.
   - Collides with nitrogen to produce carbon-11 ($^{11}$CO$_2$).
   - PET isotopes and their half-lives:
     - Carbon-11: 20.4 min
     - Fluorine-18: 109.8 min
     - Nitrogen-13: 9.97 min
     - Oxygen-15: 2.03 min

2. **Chemistry, Purification, & Formulation**

   - Conversion of carbon-11 charged particles into tracers.
   - Processes include: HPLC Purification, Rotovap Concentration, Sterile Formulation.
   - Timing:
     - ~20 min, ~40 min, ~90 min

3. **Imaging and Analysis**

   - Imaging with PET scans, analyzing γ emissions.
   - Imaging time:
     - ~60 min, ~120 min, ~90 min
Two strategies pervade PET imaging

Receptor/Ligand-based

Enzyme/Substrate-based

examples:

Raclopride – D2 receptors

FDG – Glucose Metabolism
Molecular Targets for Imaging

Enzyme Activity

Substrates

Inhibitors

Reporter Probe = Commonly Enzyme Substrate
(could also be a receptor ligand)

Glucose Metabolism

Receptors / Proteins

Ligands (e.g. small molecule, peptide, mAb)

Protein Synthesis

Viral Vector

Reporter Gene Expression

DNA

mRNA

PROTEIN SYNTHESIS

FDG

GLUT

HK

ENZ

*AA
A quick look at binding potential

PET signal is proportional to the density (but not only density)
A quick look at binding potential

These systems now have the same number of *available receptors* and thus could give the same PET signal (depending on kinetics).
Specific (radio)activity can be critical

Specific Activity is the Ratio of Hot to Cold

- **Radioactive (Hot)**
- **Nonradioactive (Cold)**

High Density Target

**High SA for PET**

Low Density Target

**Low SA for PET**
Specific (radio)activity can be critical

- If we assume that an injection (10 mCi or 370 MBq) of a PET agent is constant, then SA is really defined by the **MASS**.

- For high SA studies, we only have to inject a microgram (or so) of total mass, most of which is still non-radioactive.

- For most ligand-receptor studies, you need to have high SA. These studies are prone to saturation.

- To understand a drug’s PK, it is best to work at low SA. Microdoses do not necessarily scale linearly with dose.

- SA is time-dependent!!!
Positron-emitting isotopes & my bias today

- For today’s lecture I will be ignoring most of the periodic table. I’ll be focusing on methods to label molecules with carbon-11 and fluorine-18.
Cyclotron produced: $^{18}\text{O}(p, n)^{18}\text{F}$

H$_2^{18}\text{O}$ (enriched water) $\rightarrow$ $^{18}\text{F}$-fluoride ion ($^{18}\text{F}^-$)

### Key Considerations

- $[^{18}\text{F}^{-]}$-fluoride is produced in water, but most fluoride chemistry does not work in the presence of water
  - **Remove water**

- Fluoride is a poor nucleophile
  - **Use highly activated precursors**

- Fluoride has low solubility in organic solvents
  - **Use ‘large/soft’ cations**

- Fluoride is everywhere! Although the theoretical specific activity is 1710 Ci/µmol, we can typically achieve ~5 Ci/µmol
  - **Minimize volume**
Practical Considerations with Fluoride

How do you get rid of water?

1) Concentrate fluoride with an anion exchange column.

2.4 mL  +  \[ \text{N}^{+} \text{F}^{-} \]  \[ \text{N}^{+} \text{F}^{-} \]  \( < 0.2 \text{ mL} \)

2) Azeotrope with organic solvent

<table>
<thead>
<tr>
<th>Cosolvent</th>
<th>BP °C</th>
<th>AZ °C</th>
<th>% Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethanol</td>
<td>78.4</td>
<td>78.1</td>
<td>4.5</td>
</tr>
<tr>
<td>methanol</td>
<td>64.7</td>
<td></td>
<td>no azeotrope</td>
</tr>
<tr>
<td>n-propanol</td>
<td>97.2</td>
<td>87.7</td>
<td>28.3</td>
</tr>
<tr>
<td>isopropanol</td>
<td>82.5</td>
<td>80.4</td>
<td>12.1</td>
</tr>
<tr>
<td>acetonitrile</td>
<td>82.0</td>
<td>76.5</td>
<td>16.3</td>
</tr>
<tr>
<td>acetone</td>
<td>56.5</td>
<td></td>
<td>no azeotrope</td>
</tr>
</tbody>
</table>

How do you make fluoride more nucleophilic?

Kryptofix 2.2.2 (K\(_{222}\))
Examples of Chemistry with $[^{18}\text{F}]-\text{Fluoride}$

**Aliphatic nucleophilic substitution (typically S$_\text{N}$2)**

Example

\[
\begin{align*}
\text{Ac} & \quad \text{Ac} & \quad \text{Ac} & \quad \text{OTf} & \quad \text{MeCN, 100 °C} & \quad 10 \text{ min} & \quad K^{18}\text{F}, K_{222} & \quad K_2\text{CO}_3 \\
\text{Ac} & \quad \text{Ac} & \quad \text{Ac} & \quad 18\text{F} & \quad \text{NaOH} & \quad \text{OH} & \quad \text{OH} & \quad 18\text{F} \\
\end{align*}
\]

LG = -OTf, -OTs, Hal

**Aromatic nucleophilic substitution (typically S$_\text{N}$Ar)**

Example

\[
\begin{align*}
\text{Cl} & \quad \text{NO}_2 & \quad \text{LG} & \quad K^{18}\text{F}, K_{222} & \quad K_2\text{CO}_3 \\
\text{Cl} & \quad \text{OH} & \quad \text{OH} & \quad ^{18}\text{F} \\
\end{align*}
\]

LG = -NO$_2$, -N$_\text{+}$, -I$_\text{Ar}$

EWG = -NO$_2$, -CN, -R
Radiotracer Chemistry with Fluorine

Cyclotron produced: $^{18}\text{O}(p,n)^{18}\text{F}$ or $^{20}\text{Ne}(d,\alpha)^{18}\text{F}$

$^{18}\text{O}_2$ (enriched gas) $\rightarrow ^{18}\text{F}_2$ (carrier-added gas)

Key Considerations

- Electrophilic fluorination is the method of choice in ‘normal’ organic synthesis
- Very reactive (issues with selectivity)
- Not widely available

- Carrier-added / lower specific activity
- Only 50% of atoms can be incorporated (maximum radiochemical yield = 50%)

![Specific Activity Graph]

*Solín Method via $\text{CH}_3\text{F}$
Examples of Chemistry with $[^{18}\text{F}]-\text{Fluorine}$

**Fluoro-destannylation**

**Example**

```
\begin{align*}
\text{SnMe}_3 & \xrightarrow{^{18}\text{F}_2} \text{Boc} \xrightarrow{\text{HI}} \text{NH}_2
\end{align*}
```

Method to label electron rich aromatic rings.

**Direct Fluorination of Aromatic Rings / Alkenes**

**Example**

```
\begin{align*}
\text{AcOH} & \xrightarrow{^{18}\text{F}_2} \text{NH}
\end{align*}
```

Can be difficult to control selectivity.
L-DOPA is the precursor to the neurotransmitters dopamine, norepinephrine, and epinephrine.

- L-DOPA crosses the protective blood-brain barrier, whereas dopamine itself cannot
- Converted into dopamine by the enzyme aromatic L-amino acid decarboxylase
- Insufficient dopamine biosynthesis in the dopaminergic neurons can cause Parkinson's disease

Enzyme/substrate-based strategies are LESS sensitive to specific activity.
Cyclotron produced: $^{14}\text{N}(p,\alpha)^{11}\text{C}$

$\text{N}_2$ (high pressure gas) $\rightarrow^{11}\text{CO}_2$ or $^{11}\text{CH}_4$ in $\text{N}_2$

**Key Considerations**

- 0.2 mol of CO$_2$ in LITERS of N$_2$ (trace O$_2$) Gas
- Approximately 1/2000 ratio of $^{11}\text{C}/^{12}\text{C}$ to start and $^{11}\text{CO}_2$ is everywhere (easy to ruin SA)
- Many phase transfers are necessary and losses can occur during each
- Total reaction and purification must be ~40 min (max) from EOB

**Trap and release**
- Closed systems, pure gasses
- Tight control of flow and temperature
- Automate efficiently
Tuberculosis (TB) is the leading cause of death in the world from a bacterial infectious disease
Four frontline drugs are used for treatment, but surprisingly little is known about their PK and distribution.

**Example of Radiolabeling Drugs**

- **Rifampicin**
- **Pyrazinamide**
- **Isoniazid**
PET Imaging Predicts Relative CNS Efficacy

Summed images, baboon brain (15-90 min)

Steps to Develop a PET Radiotracer

Evaluate whether binding is specific – Radiolabeled Drug doesn’t equal Radiotracer!!
How to measure *specific* binding.

**Baseline Experiment**

**Specific Binding**

intravenous injection (+ time)

**Nonspecific Binding**
How to measure specific binding.

Pretreatment Experiment

1) intravenous injection (+ time)
How to measure *specific* binding.

Pretreatment Experiment

\[ \text{Specific Binding} = \text{Pretreatment Experiment} - \text{Specific Binding} \]
How to determine if a radiotracer is selective

Knockout Mouse

Sensitivity to Other Drugs
Carbon-11 radiotracers are prepared primarily through reactions with $[^{11}\text{C}]$methyl iodide.
A look at PET imaging of Neurotransmission!!

- Raclopride
- Dopamine (DA)
- Dopamine (D₂) receptors
- Dopamine transporters
Note: Our discussion will ignore some important characteristics of PET imaging and analysis including specific activity, changes in blood flow, arterial input, specific vs non-specific binding, and kinetic modeling.
[\textsuperscript{11}C]Raclopride Imaging: Bolus

- raclopride
- dopamine
- dopamine (D\textsubscript{2}) receptors
- dopamine transporters
$[^{11}\text{C}]\text{Raclopride Imaging: Bolus}$

- raclopride
- dopamine
- dopamine (D$_2$) receptors
- dopamine transporters
[¹¹C]Raclopride Imaging: Bolus

Raclopride (R) binds to dopamine (D₂) receptors with a high binding potential, resulting in a low binding potential for dopamine transporters. The graphic illustrates the interaction with dopamine (DA) neurotransmitters in the synaptic cleft.
[\textsuperscript{11}C]Raclopride Imaging: Bolus

- Amphetamine
- Raclopride
- Dopamine
- Dopamine (D\textsubscript{2}) receptors
- Dopamine transporters
[\textsuperscript{11}C]Raclopride Imaging: Bolus

- **A**: amphetamine
- **R**: raclopride
- **DA**: dopamine
- **D\textsubscript{2}**: dopamine (D\textsubscript{2}) receptors
- **DA** transporters
[\textsuperscript{11}C]Raclopride Imaging: Bolus

- **DA** dopamine
- **DA** dopamine transporters
- **R** raclopride
- **A** amphetamine
- **D\textsubscript{2}** dopamine (D\textsubscript{2}) receptors
- **R** dopamine transporters
[¹¹C]Raclopride Imaging: Bolus

Study Design:

- **A**:amphetamine
- **R**:raclopride
- **DA**:dopamine
- **D₂**:dopamine (D₂) receptors
- **transporters**:dopamine transporters
[\textsuperscript{11}C]Raclopride Imaging: Bolus

Study Design:

- \textbf{A}: amphetamine
- \textbf{R}: raclopride
- \textbf{DA}: dopamine
- \textbf{D}_2: dopamine (D\textsubscript{2}) receptors
- \textbf{BP}: dopamine transporters
Modafinil Blocks Dopamine Transporter

- Modafinil is a wakefulness promoting drug that is used off label as a cognitive enhancer.
- Its precise mechanism of action is unknown, but preclinical evidence suggested a role of dopamine in addition to hypocretin, histamine, epinephrine, GABA, and glutamate.

What will happen if we perform the study where we want to observe dopamine release kinetics? Perhaps something to consider as useful for an MR-PET experiment!

- amphetamine
- raclopride
- dopamine
- dopamine (D<sub>2</sub>) receptors
- dopamine transporters
[\textsuperscript{11}C]Raclopride Imaging: Bolus

Study Design:

- \textbf{R} raclopride
- \textbf{A} amphetamine
- \textbf{DA} dopamine
- \textbf{D} dopamine \((D_2)\) receptors
- \textbf{L} dopamine transporters
[\textsuperscript{11C}]Raclopride Imaging: Bolus

Study Design:

- **A**: amphetamine
- **R**: raclopride
- **DA**: dopamine
- **Dopamine (D\textsubscript{2}) receptors**
- **Dopamine transporters**
[\textsuperscript{11}C]Raclopride Imaging: B + I

Study Design:

Bolus + Infusion technique can increase the sensitivity of PET to signal change.

- Amphetamine
- Raclopride
- Dopamine
- Dopamine (D\textsubscript{2}) receptors
- Dopamine transporters
**[^{11}C]Raclopride Imaging: B + I**

Study Design:

- **R**: raclopride
- **A**: amphetamine
- **DA**: dopamine
- **Dopamine (D₂) receptors**
- **Dopamine transporters**
[\textsuperscript{11}C]Raclopride Imaging: B + I

Study Design:
Moving PET Radiotracers into Man

FDA Exploratory IND Guidance

1. Clinical studies of pharmacokinetics or imaging

Microdose studies are designed to evaluate pharmacokinetics or imaging of specific targets and are designed not to induce pharmacologic effects. Because of this, the risk to human subjects is very limited, and information adequate to support the initiation of such limited human studies can be derived from limited nonclinical safety studies. A microdose is defined as less than 1/100th of the dose of a test substance calculated (based on animal data) to yield a pharmacologic effect of the test substance with a maximum dose of <100 micrograms (for imaging agents, the latter criterion applies).\textsuperscript{15} Due to differences in molecular weights as compared to synthetic drugs, the maximum dose for protein products is ≤30 nanomoles.

- up to 0.750 - 4.5 mg for scFV - antibody products

- 5 mCi of 500 Ci/mmol radiotracer = 10 nmol
  200-300 g/mol = 2-3 micrograms

eIND is an great way to move high specific activity radiotracers into people
Moving PET Radiotracers into Man

New Molecular Entity?
- YES → Tracer Dose?
  - YES → eIND 21 CFR 312
  - NO → IND (Phase I) 21 CFR 312

- NO → Prior Human Use?
  - NO → Isotope Substitution?
    - NO → Clinical Trail?
      - NO → IND (Phase I) 21 CFR 312
      - YES → RDRC 21 CFR 361.1
    - YES → Tracer Dose?
      - YES → eIND 21 CFR 312
      - NO → IND (Phase I) 21 CFR 312
Simultaneous MR-PET Imaging at Martinos

High Resolution BrainPET (MR-PET)

Biograph mMR Whole Body (MR-PET)
Radiotracers Available for MR-PET (Human)
(also available for NHP and rodent imaging)

FDG is the most commonly used clinical PET tracer. It is partially processed in the body's glycolytic pathway, and is therefore an excellent imaging agent for glucose metabolism. FDG is commonly used for the diagnosis and treatment monitoring of several cancers and has a wide variety of other uses including blood flow monitoring and Alzheimer's diagnosis.

Diprenorphine is a high-affinity, non-selective (but mostly mu) opioid antagonist. As an imaging agent, it has been used to look at drug dependency and the body's response to pain and analgesics.

PBR28 binds selectively to peripheral benzodiazepine receptor (PBR), which is a translocator protein that is highly expressed in activated microglia. PBR has been linked to neuronal injury, and PBR28 is currently being explored as an imaging agent for inflammation in the brain, as well as other tissues throughout the body.

http://hookerlab.martinos.org/tracers/
# CNS Radiotracer Table

**CNS Radiotracers that have been advanced for use in Human Studies**

<table>
<thead>
<tr>
<th>Molecular Target</th>
<th>$^{11}$C-Labeled ligand</th>
<th>$^{18}$F-Labeled ligand</th>
<th>$^{123}$I-Labeled ligand</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aggregated protein target</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Amyloid</td>
<td>$[^{11}]$C-PiB</td>
<td>$[^{18}]$F-Flutemetamol</td>
<td>$[^{123}]$I-NPIY</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$[^{18}]$F-Florbetapir(18F)AV-45</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$[^{18}]$F-AZD 4694</td>
<td></td>
</tr>
<tr>
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<td></td>
<td>$[^{18}]$F-FBM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$[^{18}]$F-FDDNP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$[^{18}]$F-SMBR-W372 (F-18)-W372</td>
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</tr>
<tr>
<td></td>
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<td>$[^{18}]$F-Florbetaben</td>
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<tr>
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<td>$[^{18}]$F-MK3328</td>
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<tr>
<td>Tau/Synuclein</td>
<td>$[^{18}]$F-8F-227</td>
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</tr>
<tr>
<td></td>
<td>$[^{18}]$F-THK523</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Channel target</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

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User Fees for Research Imagers

MR-PET studies can vary widely in design and cost. To best serve the MR-PET user community, we have developed a flexible method to price studies fairly. You can use the information below to estimate your per-study charges, but you should verify your estimate with Jacob Hooker (hooker@nmr.mgh.harvard.edu) before budgeting for a study. Example prices here capture the most common experiments.

<table>
<thead>
<tr>
<th>Current Rates</th>
<th>Anticipated rates for FY14 (beginning Oct 1, 2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG Dynamic Scan</td>
<td>$2159 (includes 1.5 h MR-PET time, FDG, nuc med support, and image preprocessing)</td>
</tr>
<tr>
<td>C-11/F-18 Dynamic Scan</td>
<td>$3442 (includes 1.5 h MR-PET time, radiotracer synthesis, nuc med support, and image preprocessing)</td>
</tr>
<tr>
<td>C-11/F-18 Dynamic Scan with Blood</td>
<td>$4117 (includes items above plus blood analysis)</td>
</tr>
<tr>
<td>O-15 CBF study</td>
<td>$3817 (includes 1.0 h of MR-PET time, producing 15O-water, blood work, nuc med support, and image preprocessing)</td>
</tr>
</tbody>
</table>

Here's how we arrive at these numbers. Please work with us to make sure your budget is correct before using it in a grant application.

Anticipated rates for FY14 are noted in parentheses, in red text. 2014 rates begin Oct 1, 2014.

MR-PET scan time: $588/hr (same)

This now matches the other large-bore scanner fees. Whether you are doing MR only, PET only, or MR-PET the rate per hour is the same. Be mindful of set-up and breakdown time, which is generally longer for PET-containing studies than for MR-only studies.

Provide FDG: $442/scan ($476/scan)

The MR-PET facility team will arrange for the delivery of FDG for your study to Bay 6, Bay 7, or mPET. This cost includes the cost of FDG from a commercial source as well as the labor associated with radioactivity log documentation. Some users (particularly for animal studies) may choose to prepare for FDG on their own. To ensure human studies to run...
Molecular Imaging and Contrast Agent Database (MICAD)
http://www.ncbi.nlm.nih.gov/books/NBK5330/
ClinicalTrials.gov is a registry and results database of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals. Read more...

Search for Clinical Trials

Find trials for a specific medical condition or other criteria in the ClinicalTrials.gov registry. ClinicalTrials.gov currently has 124,453 trials with locations in 179 countries.

Investigator Instructions

Get instructions for clinical trial investigators/sponsors about how to register trials in ClinicalTrials.gov. Learn about mandatory registration and results reporting requirements and US Public Law 110-85 (FDAAA).

Background Information

Learn about clinical trials and how to use ClinicalTrials.gov, or access other consumer health information from the US National Institutes of Health.
https://scifinder.cas.org

SciFinder

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New SciFinder Enhancements Improve Workflow to Help You Make Better Synthetic Research Decisions Faster

We are pleased to announce that SciFinder, the world’s best chemistry research tool, has been enhanced with new content additions that align with your workflows to help you make better synthetic research decisions faster.

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