Molecular Imaging Technologies: from Cells to Humans

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Imaging Technologies
Information Content

Tag specific information, relevant to the state of the process

Imaging can not only visualize, but quantitate the relevant process
Molecular Imaging Targets/Probes

- Receptor Mapping
  - Accumulation via MAb, Fragments
  - Hormones
  - Drugs and Ligands
  - Peptides
- Enzyme Activity:
  - Inhibition, Concentration, Synthesis
- Accumulation via Phosphorylation
  - $[^{18}F]$FDG
- DNA Accumulation via DNA-Synthesis
- mRNA Accumulation via AA Transport or Protein Synthesis
- Oligonucleotides mRNA Binding
- Internalization
- Reporter Gene
- Reporter Probe
- Hexokinase
- glut 4
- MAb, Fragments
- mRNA
- DNA
- AAT
- Enzyme Activity: Inhibition, Concentration, Synthesis
- Accumulation via DNA-Synthesis
- Oligonucleotides mRNA Binding
Molecular Imaging Probes

Radionuclide Probes vs. Activatable Probes

TIME

TIME
Bioluminescence Imaging

Luciferase (enzyme)
+ Luciferin (substrate) → Light
+ energy

Firefly controls production of both luciferase and luciferin

Given an excess of substrate, thousands of photons can be produced per enzyme
The Imaging Chamber

- CCD Chip
- Optical Filter wheel
- Shutter
- Lens and Aperture
- Illuminator
- Heated Sample Stage
- Electronics

\[ \Omega \sim 1\% \]
\[ \text{QE} \sim 90\% \]

Graph showing peak intensity attenuation vs depth (mm).
Standard Images are composed of two datasets
Photographic + Luminescent → Overlay
Optical and PET Imaging

- Human metastatic melanoma tumor model
- triple fusion protein (luminescence, fluorescence, PET)
PET Sensitivity

- No collimators necessary: *100% efficiency possible*
  - Stopping power of 1cm LSO ~30%
  - Coincidence stopping is ~10%
  - Solid angle is ~50%
  - In practice 5-10% sensitivity

\[ P(A \cap B) = P(A) \cap P(B) = P(A) \times P(B) \]
Dynamic Range

The range of activities encompasses >10 log orders

e±/sec 10^0 10^3 10^6 10^9

1 pCi 1 nCi 1 μCi 1 mCi

High Sensitivity
• Cell cultures have uptakes on the order of pCi/cell (0.1 e±/sec)
• Phosphorylation – assays have on the order of (0.1 e±/sec)

High Flexibility
• Probe synthesis produces >mCi of activity (~10^8 e±/sec)
• In-vivo imaging >1nCi

Different technologies completely cover this large spectrum.
Microfluidics

Operation Mechanism of a Pressure-Driven Valve

Valve open

Valve close

Pressure

Flow

Microfluidics:

Chemical Synthesis
Biological Assays
Cell cultures

Key Parameters:

1. *Thin substrate* allows detection of low energy betas
2. *Thick detector* will absorb more energy from incoming betas
PSAPD Detection Limits, Linearity

**Diagram:**
- Microfluidic chip
- PSAPD

**Graph:**
- X-axis: Time (mins)
- Y-axis: Net Counts \( \text{mm}^2 \)
- Graph shows decreasing counts with time, reaching 2 pCi/mm\(^2\) and 2.9 nCi/mm\(^2\).
- Markers for F-18 Activity and MDA.

**Branding:**
- UCLA
- Crump Institute for Molecular Imaging
Cell Culture and FDG Uptake

- A549 cell line
- Loading of FDG solution into Cell Chambers
- Movie plays x6 faster than real time
Cell Culture System: Sensitivity

- 20 minute acquisition, 1mCi/cc FDG
- System can quantify the FDG uptake of 1 cell

Intracellular FDG concentration: 25nmol

![Image showing cell culture system with sensitivity graph and a bar chart indicating cell counts and FDG activity per cell.](image-url)
Translational Molecular Imaging

Molecular

In vitro

Clinic

In vivo
Small Animal PET Systems
Results (volumetric projections)

Negative control

HSV-tk positive mouse

- Time lapse movies of the tracer distribution
Results - Time Activity Curves

Coronal slices through individual frames of the time lapse movie for the HSV-tk positive mouse.
Conclusions

- Molecular Imaging “Seeks to advance our understanding of biology and medicine through noninvasive in vivo investigation of cellular molecular events involved in normal and pathologic processes” (Society of Molecular Imaging)
- Requires a mutually educating collaborative environment that includes biologists, physicists, chemists, mathematicians, physicians and clinicians
- Physicists and engineers provide expertise in the development and usage of state of the art imaging tools for biologists
- Devise and develop new tools that will answer important biological questions