Cerenkov Applications in Oncology

Nicole Ackerman

Agnes Scott College
Department of Physics

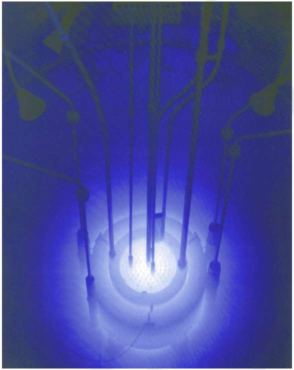
17 March 2014

Today's Talk

1. **Cerenkov Production**
2. **Pre-Clinical Imaging**
3. **Radionuclides in Medicine**
    - Positron Emission Tomography
    - Alpha and Beta: Therapy
4. **Clinical Possibilities**
    - Surface Imaging
    - External Beam
5. **Moving Forward, Conclusions**

Outline

1. **Cerenkov Production**
2. Pre-Clinical Imaging
3. Radionuclides in Medicine
   - Positron Emission Tomography
   - Alpha and Beta: Therapy
4. Clinical Possibilities
   - Surface Imaging
   - External Beam
5. Moving Forward, Conclusions



Mechanism

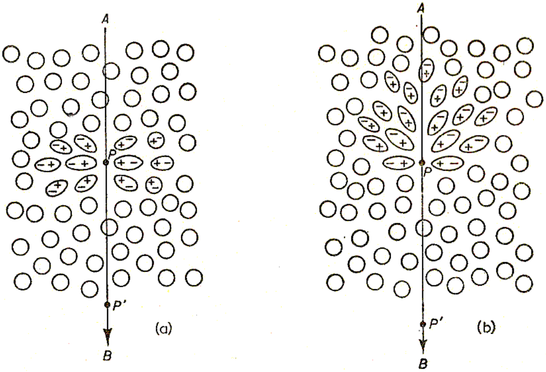


FIG. 1.1. The polarization set up in a dielectric by the passage of a charged particle. (a) At low velocity. (b) At high velocity.

From: Jelley "Čerenkov radiation and its applications" (1958)

Cerenkov Cone

$$\cos\theta = \frac{1}{\beta n}$$

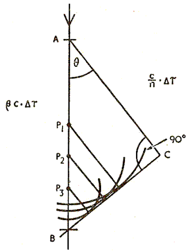
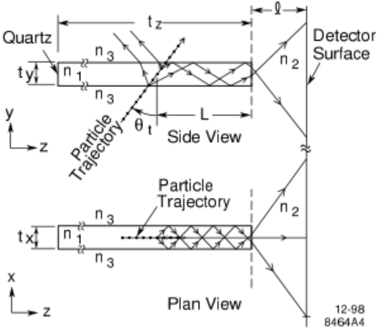


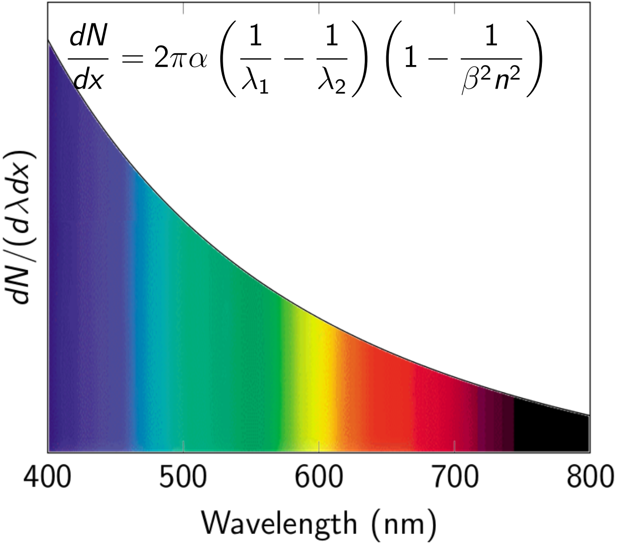
FIG. 1.2. Huygens construction to illustrate coherence.

From: Jelley "Čerenkov radiation and its applications" (1958)

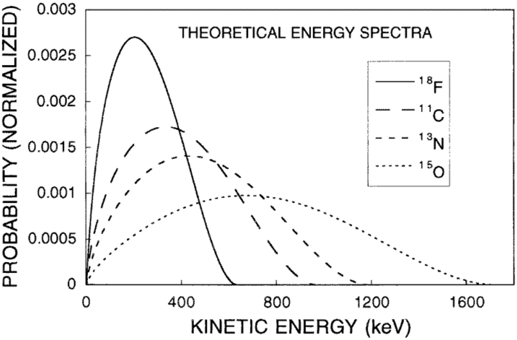


BABAR Collab. Nucl.Instrum.Meth. A538 281-357 (2005)

Emitted Spectrum



Threshold: β and n



Levin and Hoffman *Phys Med Biol* (1999)

$$\beta_{thresh} = \frac{1}{n}$$

Water:

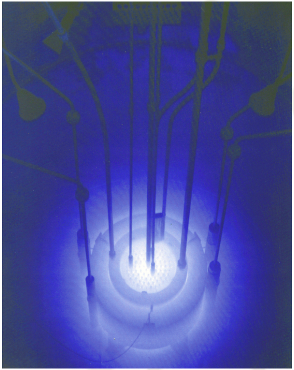
- $n = 1.33$
- $E_{thresh} = 263$ keV

Tissue:

- $n = 1.36 - 1.45$
- $E_{thresh} \approx 220$ keV

Outline

1. Cerenkov Production
2. **Pre-Clinical Imaging**
3. Radionuclides in Medicine
   - Positron Emission Tomography
   - Alpha and Beta: Therapy
4. Clinical Possibilities
   - Surface Imaging
   - External Beam
5. Moving Forward, Conclusions



Pre-Clinical Imaging

Genetics
Chemistry
Biology

↓

Cell Testing

↓

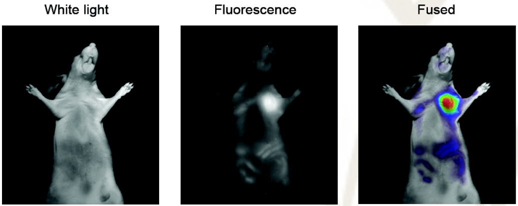
Mouse Testing

↓

First Human Tests

In Vivo Imaging:

- (+) Use same mice
- (+) Observe biodistribution
- (+) Fast, quantitative
- (+) Similar to clinical imaging
- (-) Organ-level resolution



Optical Imaging

- Use black box with CCD camera
- Common, affordable system
- Common biomedical techniques:
  - Bioluminescence
  - Fluorescence

Only Pre-clinical:

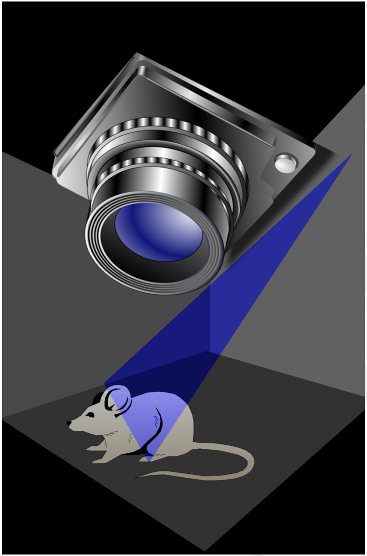
- Light Scattering
- Poor Penetration

Optical Imaging

- Use black box with CCD camera
- Common, affordable system
- Common biomedical techniques:
  - Bioluminescence
  - Fluorescence

Only Pre-clinical:

- Light Scattering
- Poor Penetration



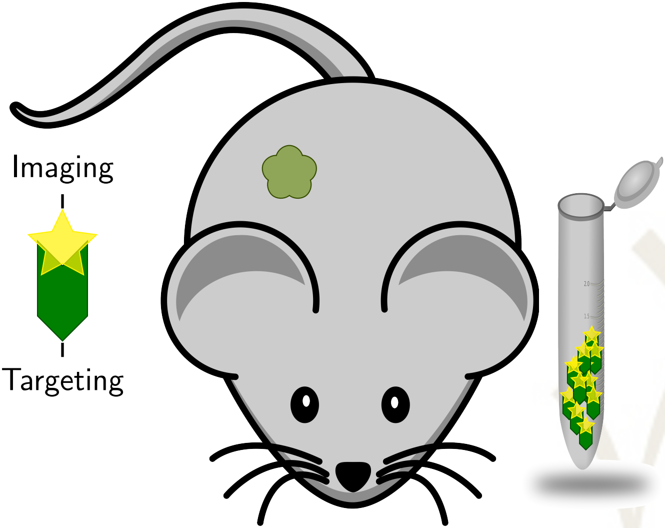
Optical Imaging

- Use black box with CCD camera
- Common, affordable system
- Common biomedical techniques:
  - Bioluminescence
  - Fluorescence

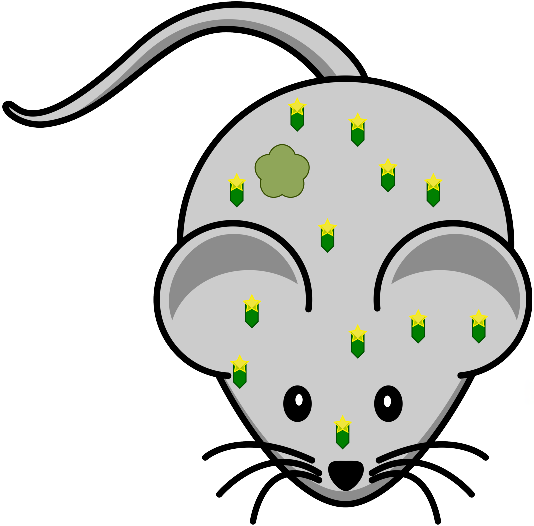
Only Pre-clinical:

- Light Scattering
- Poor Penetration

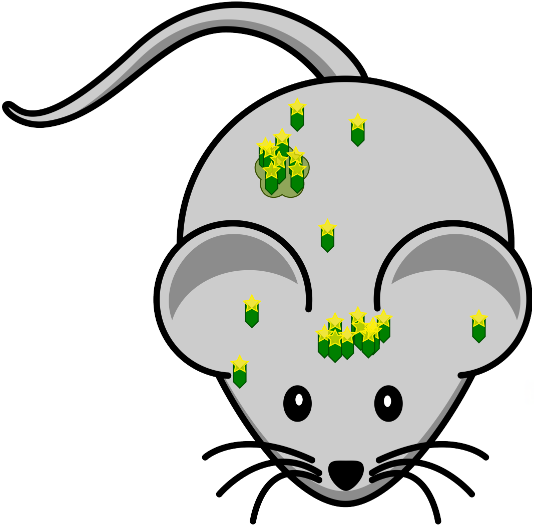
Testing Drugs in Mice



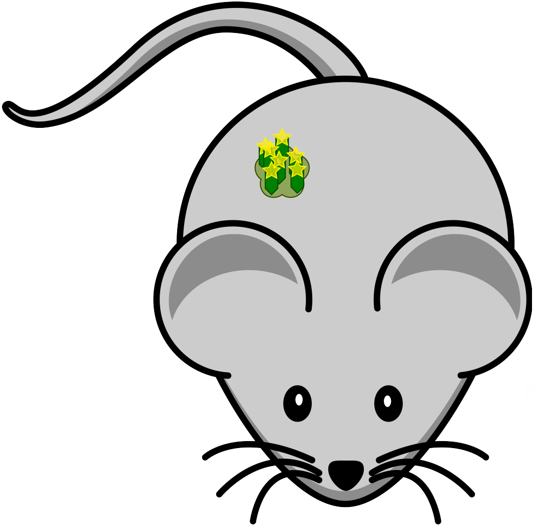
Testing Drugs in Mice



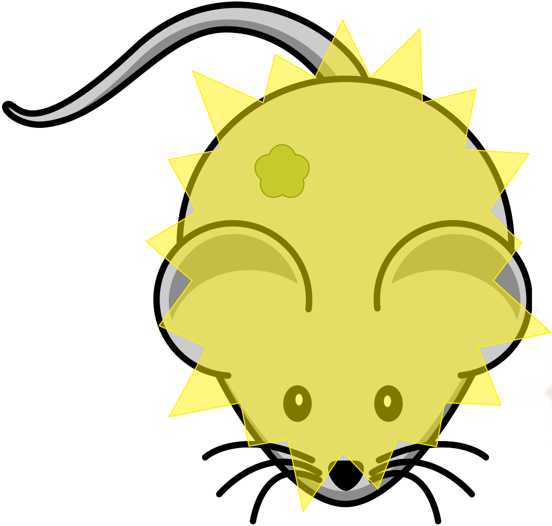
Testing Drugs in Mice



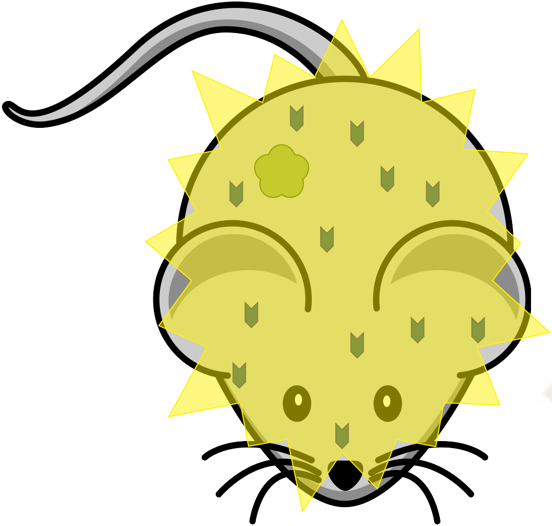
Testing Drugs in Mice



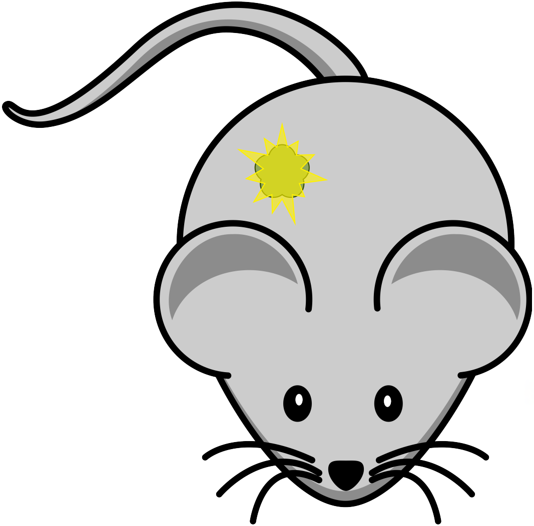
Testing Drugs in Mice



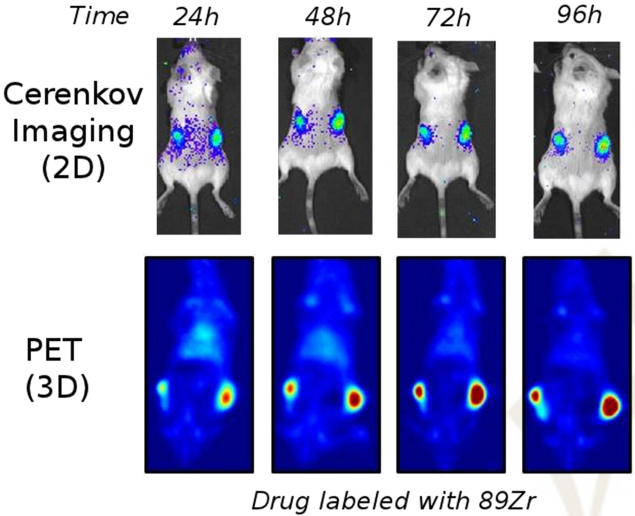
Testing Drugs in Mice



Testing Drugs in Mice

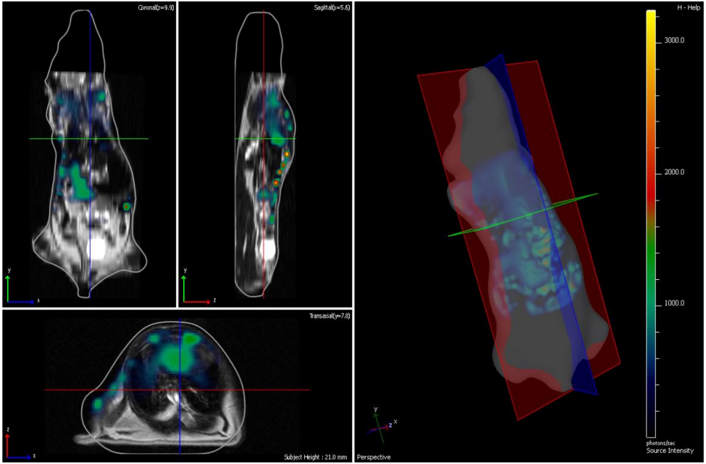


Cerenkov Luminescence Imaging



Ruggiero *et al J Nucl Med* (2010)

3-Dimensional Imaging

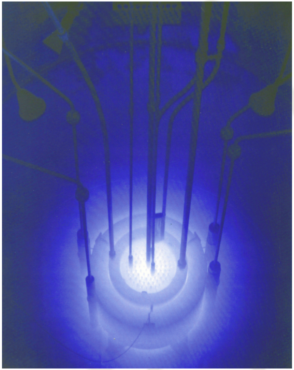


(^{32}P-ATP)

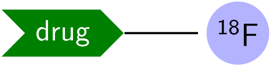
Spinelli *et al Optics Express* (2011)

Outline

1. Cerenkov Production
2. Pre-Clinical Imaging
3. **Radionuclides in Medicine**
   - Positron Emission Tomography
   - Alpha and Beta: Therapy
4. Clinical Possibilities
   - Surface Imaging
   - External Beam
5. Moving Forward, Conclusions



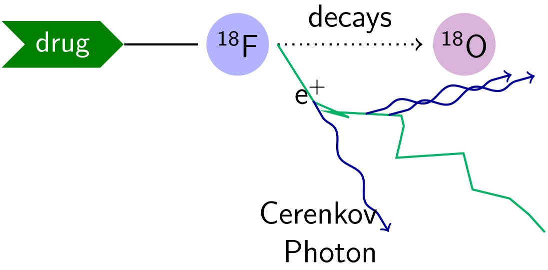
Positron Emission Tomography

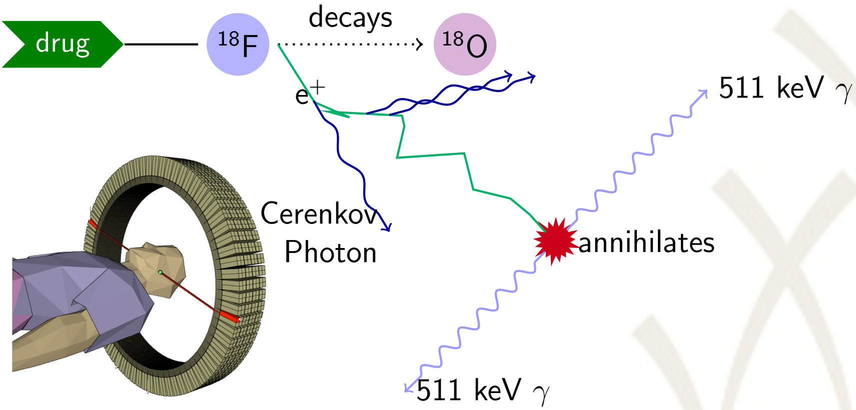


Positron Emission Tomography

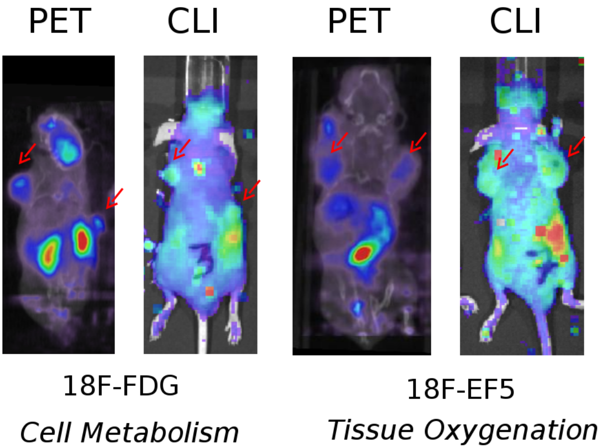
drug — $^{18}\mathrm{F} \xrightarrow{\text{decays}} {}^{18}\mathrm{O}$

Positron Emission Tomography



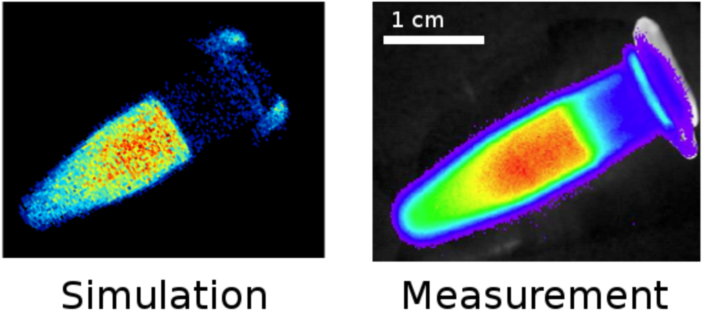

drug
^{18}F
decays
^{18}O
e^+
511 keV γ
Cerenkov
Photon
annihilates
511 keV γ

Most Common: ^{18}F-FDG



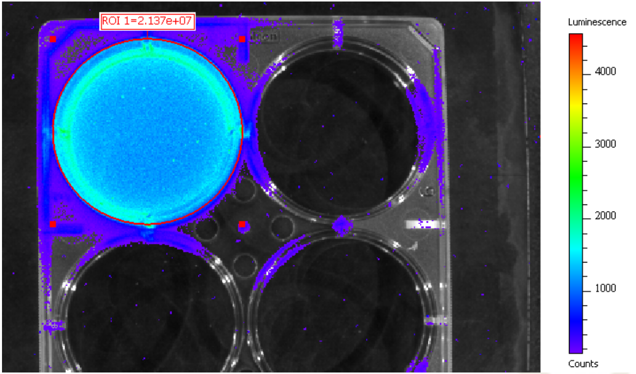
Graves Group, Stanford University

^{18}F in Geant4



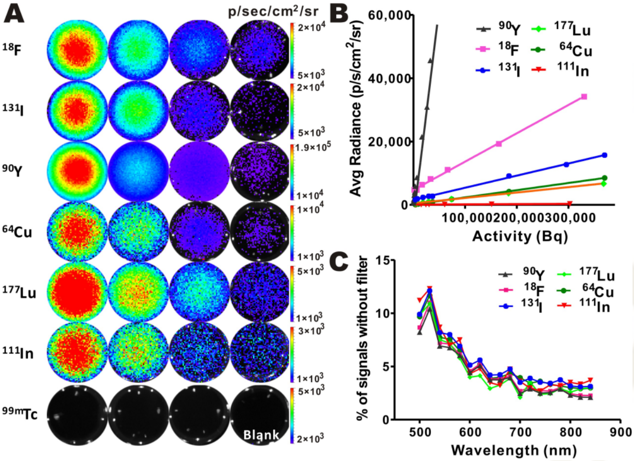
Graves Group, Stanford University

Phantom Studies



Graves Group, Stanford University

Other Isotopes



Liu *et al*, *PLoS One* (2010)

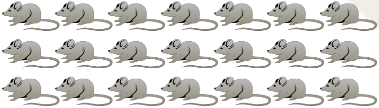
CLI vs PET

PET

$\$\$\$\$\$\$\$\$\$\$$

$^{18}F \cdots\cdots\rightarrow \beta^+$

CLI



$\$$

$^{18}F \cdots\cdots\rightarrow \beta^+$

$^{32}P \cdots\cdots\rightarrow \beta^-$

Many Isotopes Studied

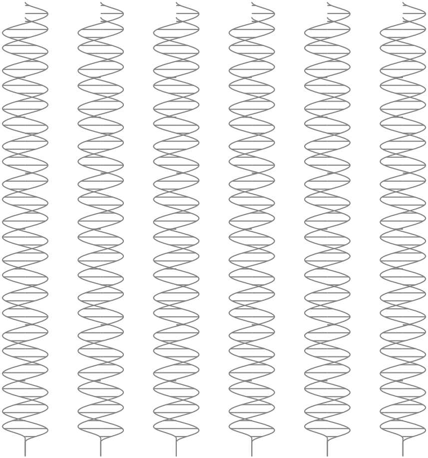
Isotope	Decay	Source
^{18}F	β^+	[1]
^{13}N	β^+	[1]
^{64}Cu	β^+	[2]
^{131}I	β^-	[2]
^{90}Y	β^-	[2]
^{177}Lu	β^-	[2]
^{111}In	EC	[2]
^{89}Zr	β^+	[3]
^{225}Ac	α	[3]
^{74}As	β^+/β^-	[4]
^{124}I	β^+	[5]
^{68}Ga	β^+	[5]
^{32}P	β^-	[5]
^{35}S	β^-	[5]

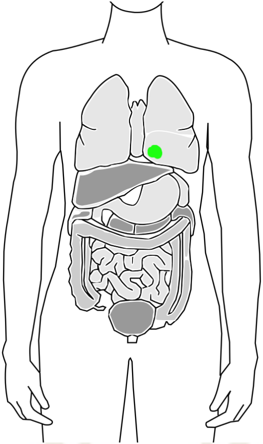
[1] Robertson et al *Phys Med Bio* 2009
[2] Liu et al *PLoS One* 2010
[3] Ruggiero et al *J Nucl Med* 2010
[4] Lewis et al *Opp Lett* 2010

[5] Park et al *Nuc Med Bio* 2010

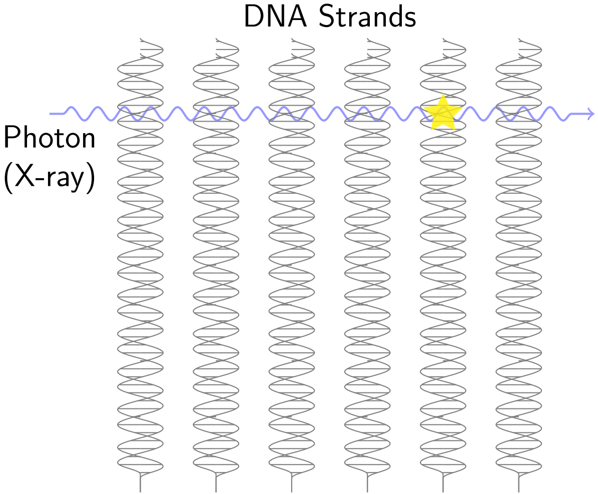
Treatment Options

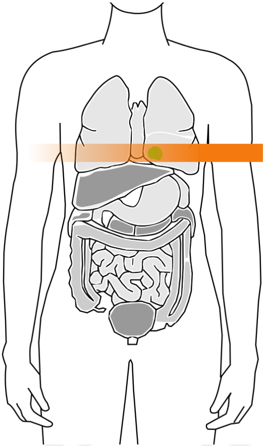
DNA Strands



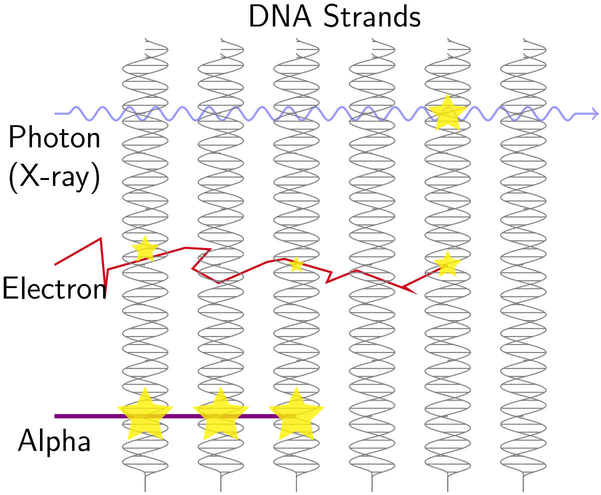


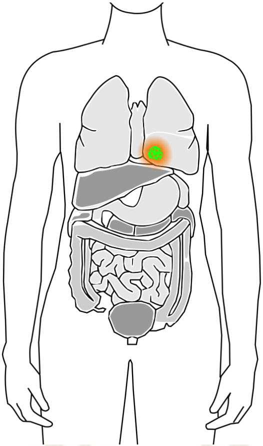
Treatment Options



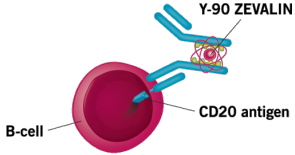


Treatment Options



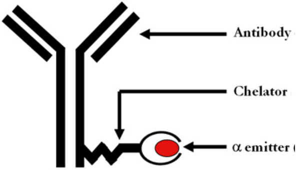


Example Drugs

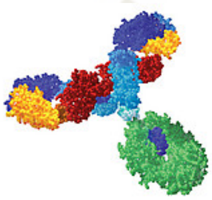


Zevalin

Monoclonal Antibody (Rituximab) for non-Hodgkin's lymphoma (NHL)



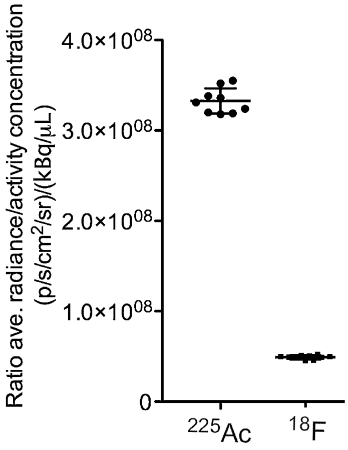
Actinium Pharmaceuticals, Inc

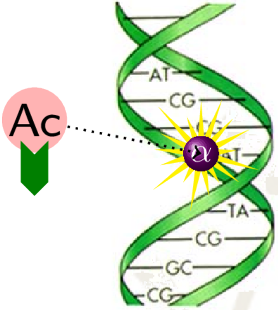


Memorial Sloan Kettering Cancer Center

Monoclonal Antibody (lintuzumab) for acute myelogenous leukemia (AML)

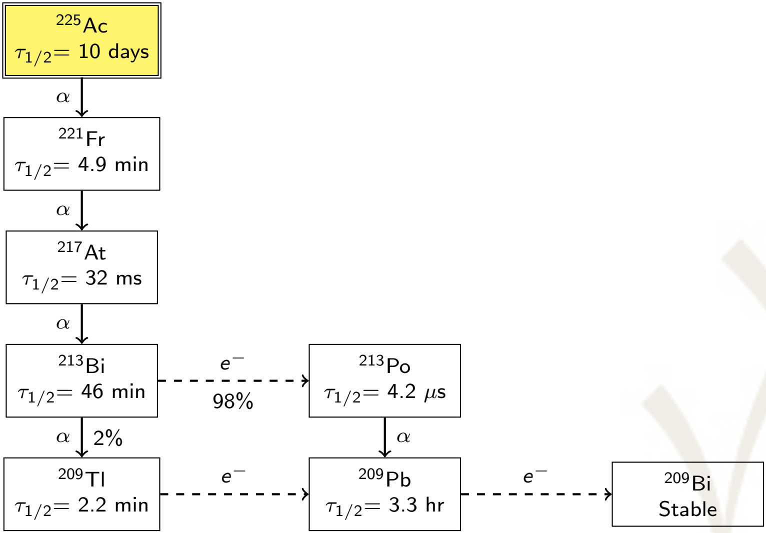
^{225}Ac For Therapy



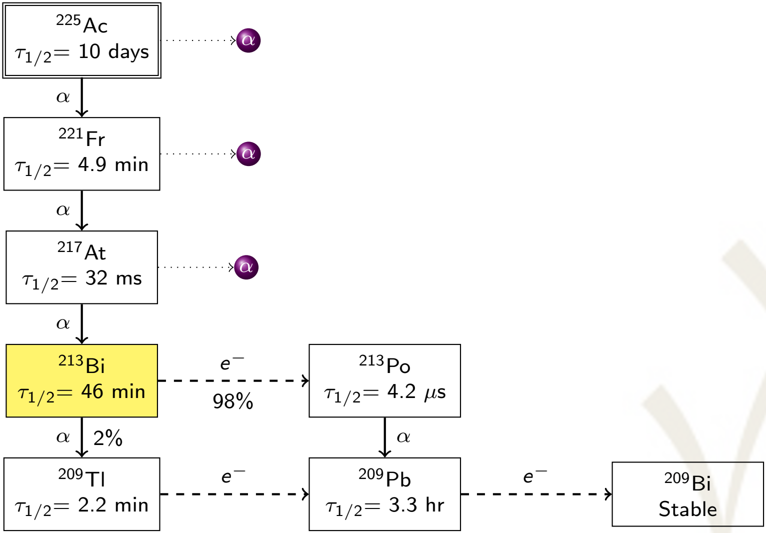


Ruggiero *et al J Nucl Med* (2010)

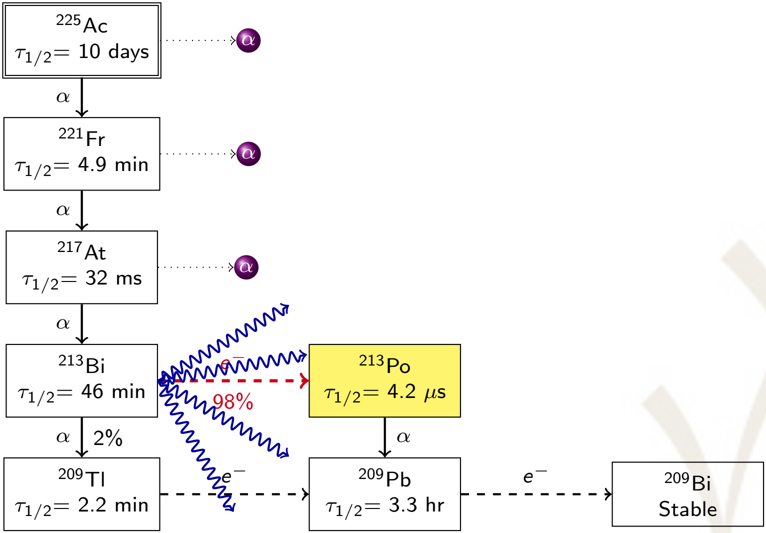
^{225}Ac Decay Chain



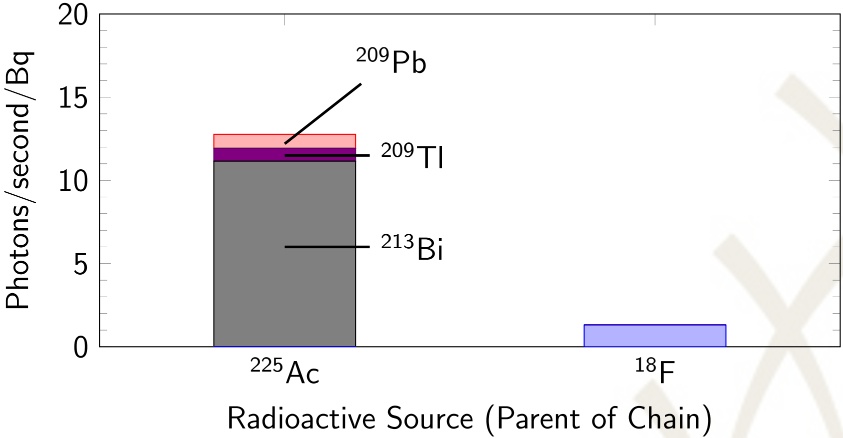
^{225}Ac Decay Chain



^{225}Ac Decay Chain



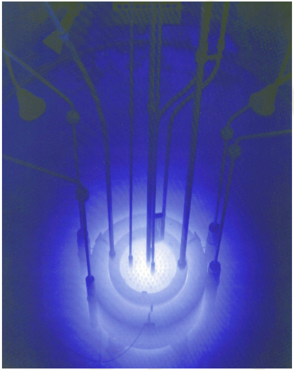
α-Emitter Cerenkov



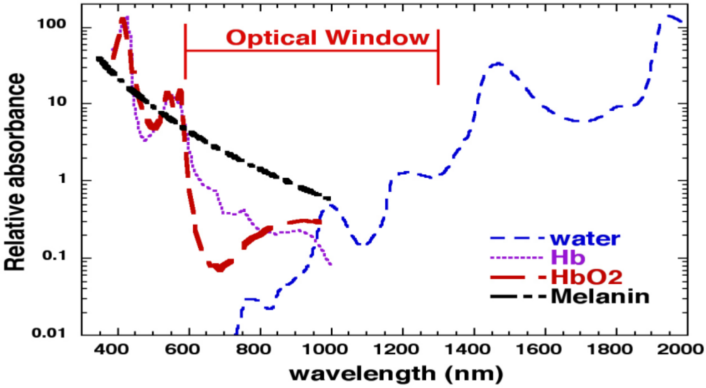
Ackerman and Graves, *Physics in Medicine and Biology* (2012)

Outline

1. Cerenkov Production
2. Pre-Clinical Imaging
3. Radionuclides in Medicine
   - Positron Emission Tomography
   - Alpha and Beta: Therapy
4. **Clinical Possibilities**
   - Surface Imaging
   - External Beam
5. Moving Forward, Conclusions

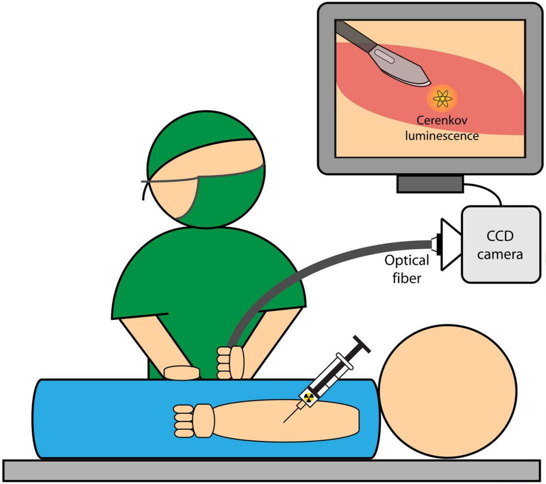


Problem: Tissue Attenuation



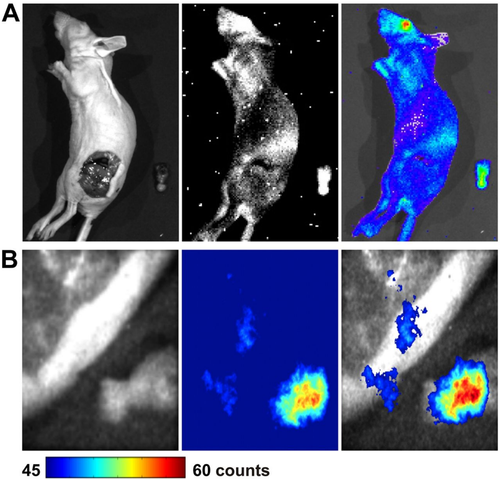
Huang *et al*, *SPIE Newsroom* (2009)

Endoscopy



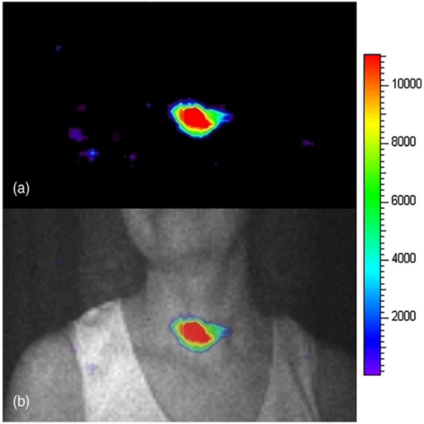
Liu *et al J Nucl Med* (2012)

During Surgery



Liu *et al J Nucl Med* (2012)

Superficial Tumors

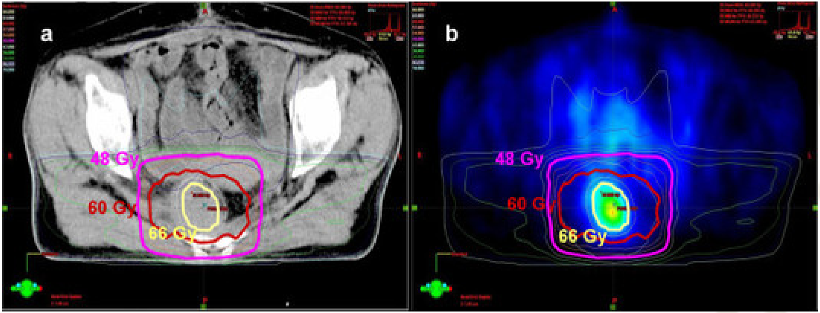


Spinelli *et al*, *J Biomed Opt* (2013)

External Beam Radiotherapy

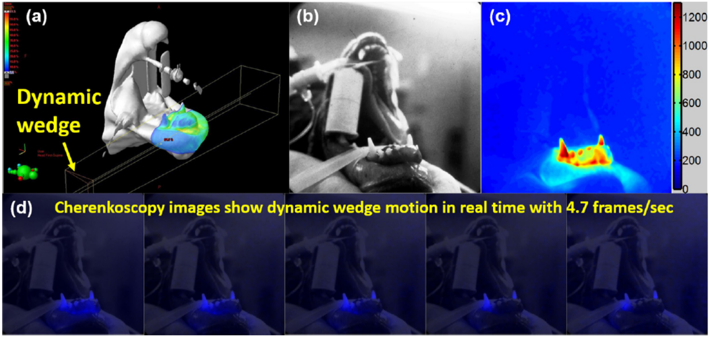
Accuray

Dose Planning



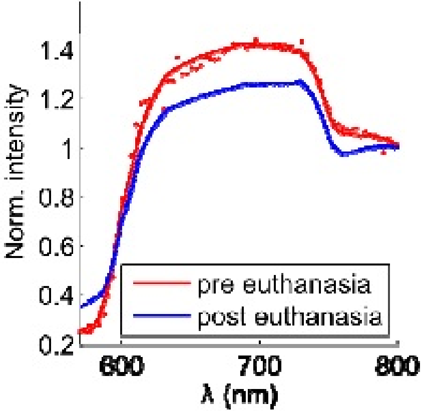
Jingu *et al*, *BMC Cancer* (2010)

Dose Monitoring



Zhang *et al*, *J Biomed Opt* (2013)

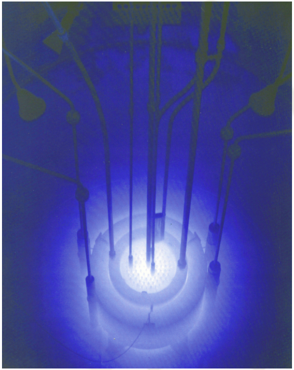
Tissue Oxygenation



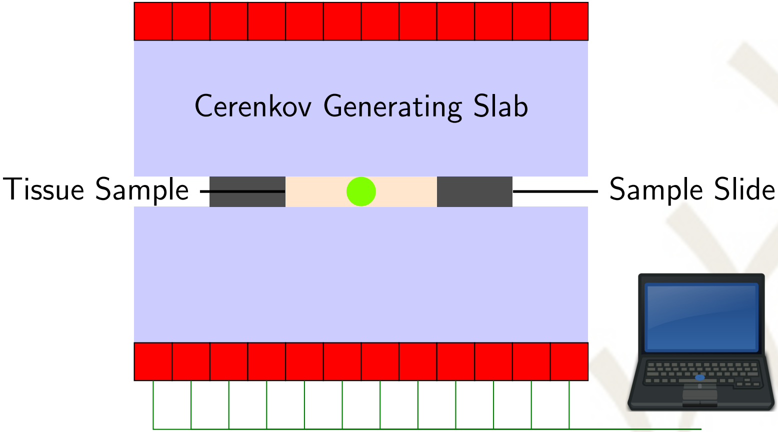
Axelsson *et al*, *Optics Express* (2012)

Outline

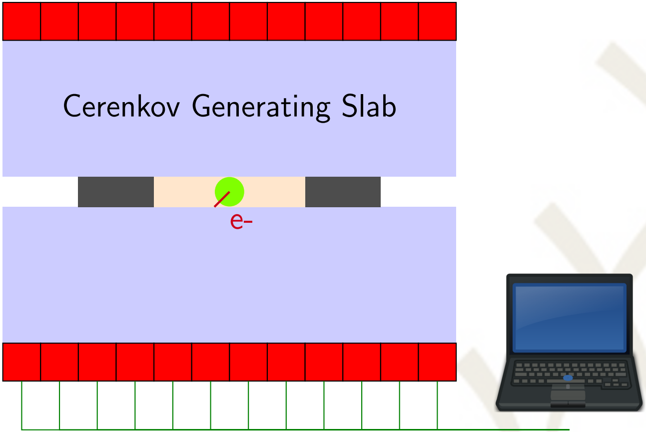
1. Cerenkov Production
2. Pre-Clinical Imaging
3. Radionuclides in Medicine
   - Positron Emission Tomography
   - Alpha and Beta: Therapy
4. Clinical Possibilities
   - Surface Imaging
   - External Beam
5. **Moving Forward, Conclusions**



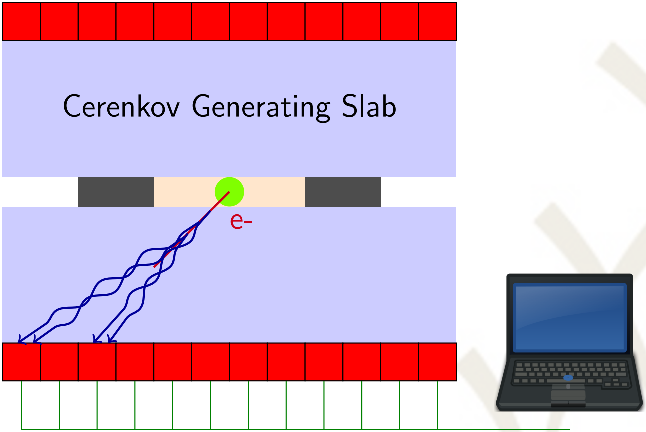
Cerenkov Microscopy?



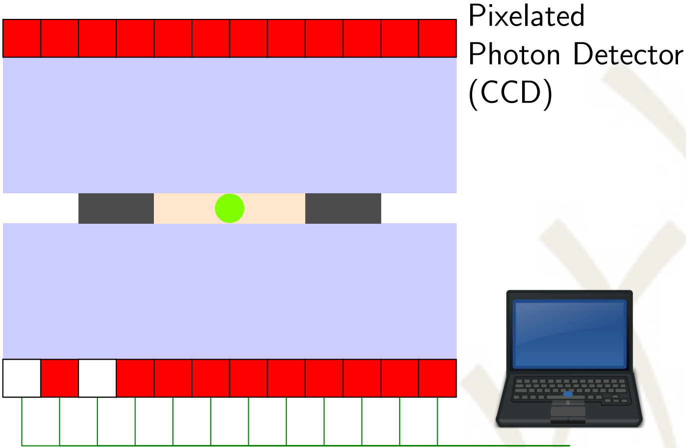
Cerenkov Microscopy?



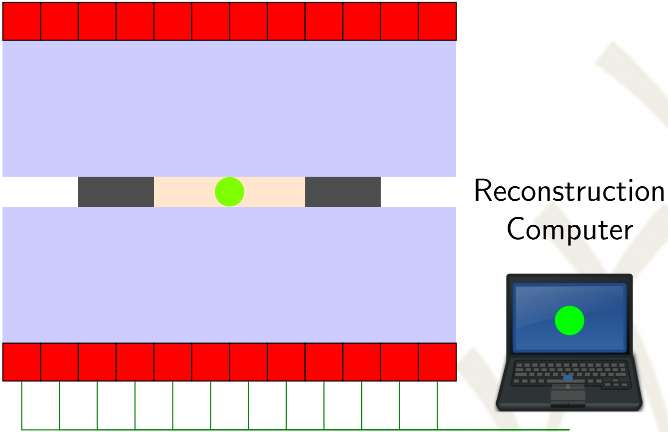
Cerenkov Microscopy?



Cerenkov Microscopy?



Cerenkov Microscopy?



Remaining Questions

- Will the ease of optical (vs nuclear) imaging benefit drug development?

Remaining Questions

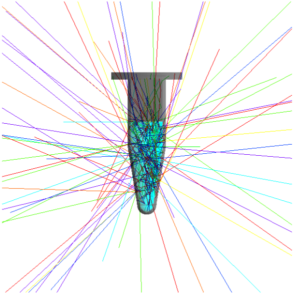
- Will the ease of optical (vs nuclear) imaging benefit drug development?
- Will better β^- and α emitting drugs be developed?

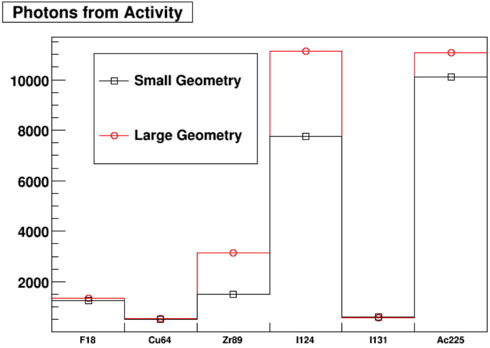
Remaining Questions

- Will the ease of optical (vs nuclear) imaging benefit drug development?
- Will better β^- and α emitting drugs be developed?
- Will Cerenkov imaging gain traction in the clinic?

Physics Contributions

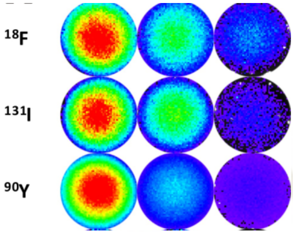
- Modeling
- Decay Fundamentals
- Secondary Parameters: Volume, Container

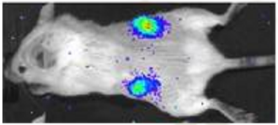


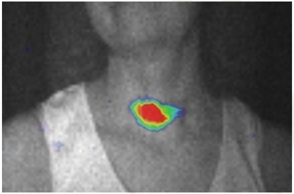


Conclusions

- Many medical isotopes produce Cerenkov
- Rapid progress in pre-clinical applications
- First clincal/human results now







Acknowledgments

Agnes Scott College

Student Collaborators:

- Kim Luong
- Melissa Hutcheson

Stanford University

Collaborators:

- Prof. Edward Graves
- Dr. Rehan (Bobby) Ali

Funding:

- Weiland Family Fellowship
- DARE Fellowship