Università di Pisa

Pre-tesi di Dottorato

XXVIII CICLO

CHERENKOV LUMINESCENCE IMAGING:
System Requirements, Experimental Setup and Potential Applications

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Overview

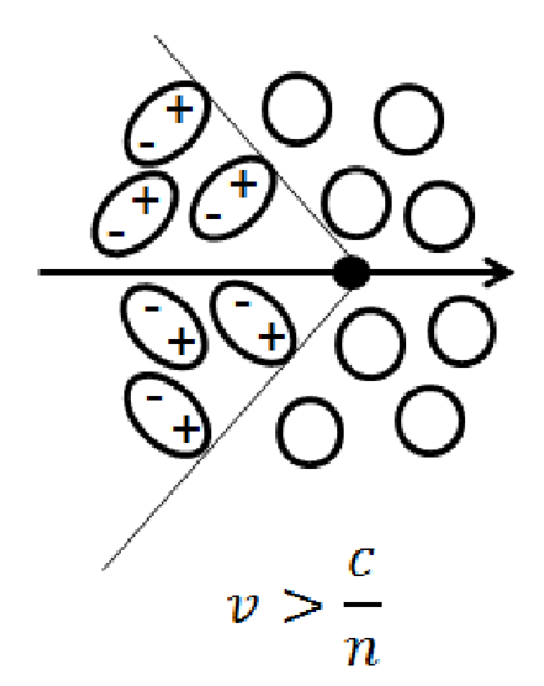
- Introduction and Theoretical background
- CLI detection system requirements
- CLI detection system setup
- Potential applications
- Collaborations
- Conclusions and Future Work

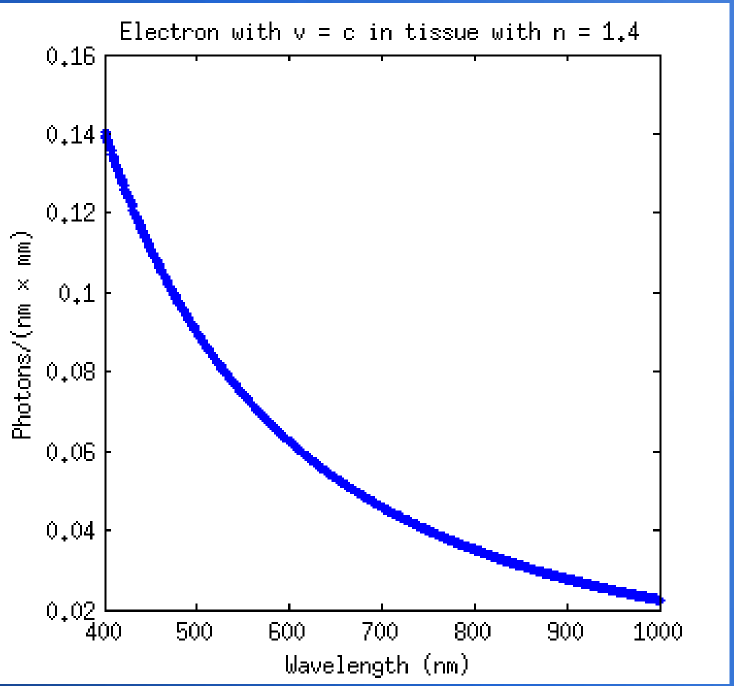
Cherenkov Radiation (CR)

- Cherenkov radiation (CR) is bluish-white light with a countinuous spectrum, emitted when a charged particle travels in a dielectric medium with a velocity greater than the speed of light in that medium
- Cherenkov relation

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

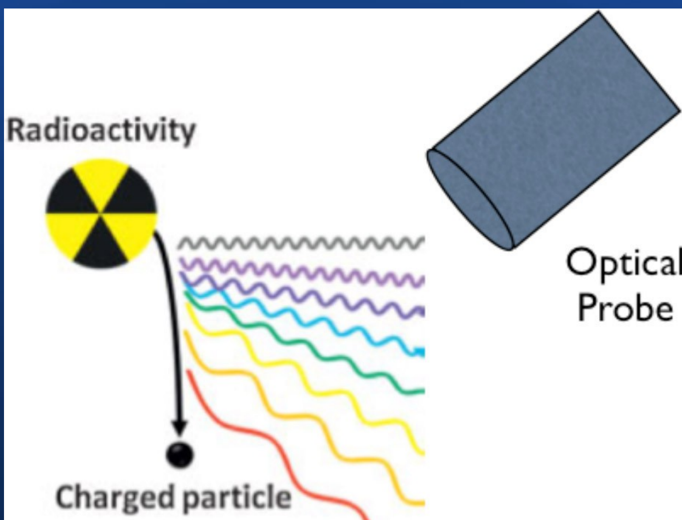
- Frank and Tamm theory: energy radiated by a particle of charge q = ze per unit track length





$$\frac{dW}{dl} = \frac{q^2}{c^2}\int_{\beta n(\omega)>1}\left(1-\frac{1}{\beta^2 n^2(\omega)}\right)\omega\, d\omega$$

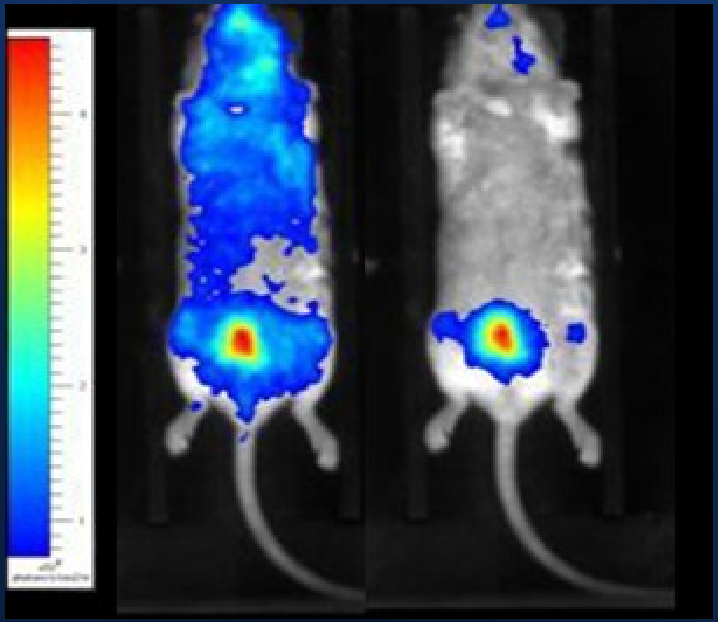
Introduction



- CLI is a recent molecular imaging technique that obtains functional informations detecting the Cherenkov radiation produced in biological tissue by the β particles emitted in the decay of radionuclides used in nuclear medicine [Mitchell et al, 2011]
- The detection is usually done using a Charge-Coupled-Device-based technology and a dedicated optics, and the experiment takes place in a dark environment to allow the detection of the very faint signal
- Advantages: ease of use, reduced cost, direct applicability to β^- emitters, widely used but conventional imaging techniques (PET, SPECT) detect γ radiation

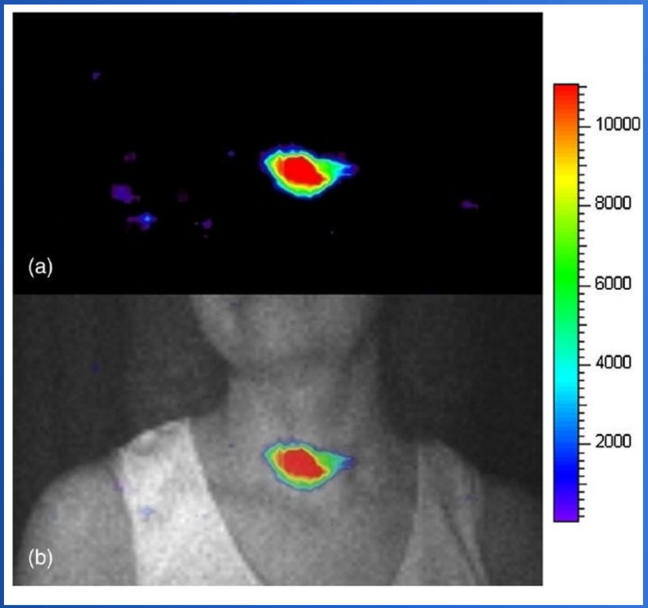
CLI State of the Art

- First feasibility studies [Ruggiero et al 2010, Zhong et al 2011] show that CLI can provide quantitative results comparable with those of SPECT and PET
- Many applications: small animal, intraoperative, endoscopy, superficial radiotherapy, proton therapy, ...



http://www.biospacelab.com/

http://www.lightpointmedical.com



doi: 10.1117/1.JBO.18.2.020502

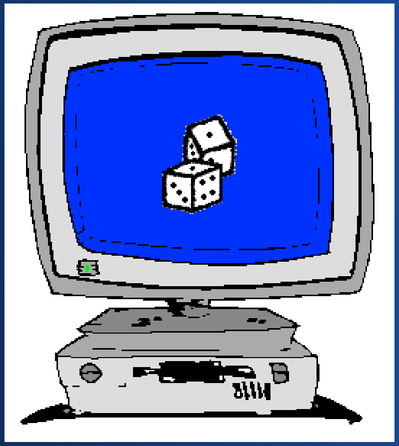
My Contribution

Already done:

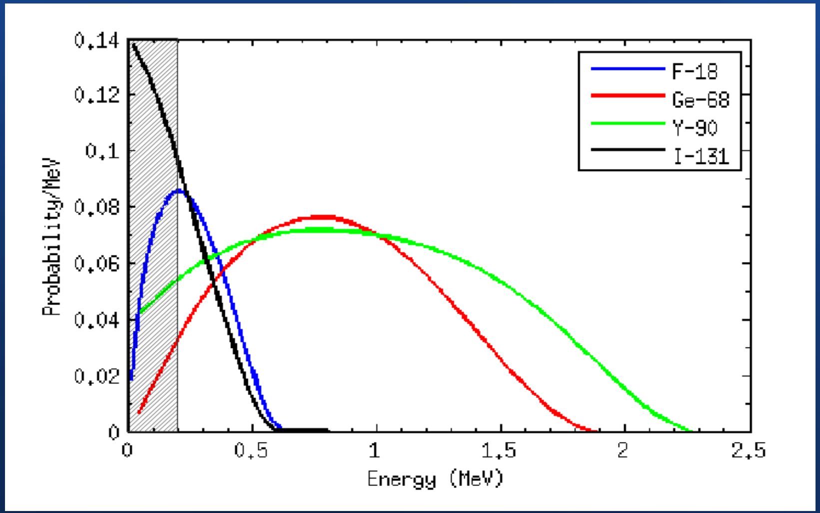
- M. Sc. Thesis: Development of a GEANT4 based Monte Carlo code for modelization of Cherenkov radiation production and transport in tissue, and partial validation

To do:

- Understanding of the requirements of a CLI detection system
- Setup of such a system
- Choice of one or some potential applications → data taking
- Monte Carlo code complete optimization and validation

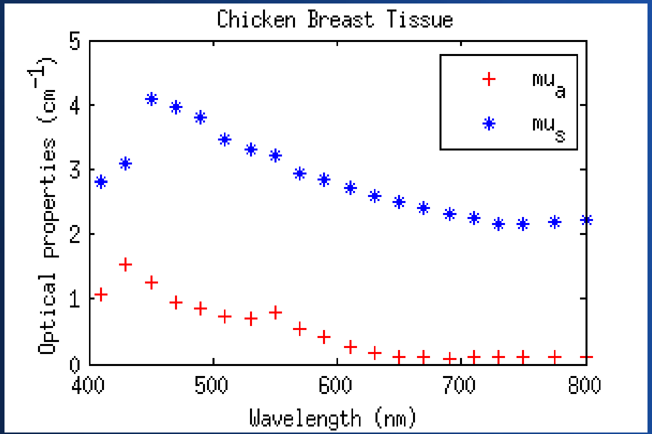


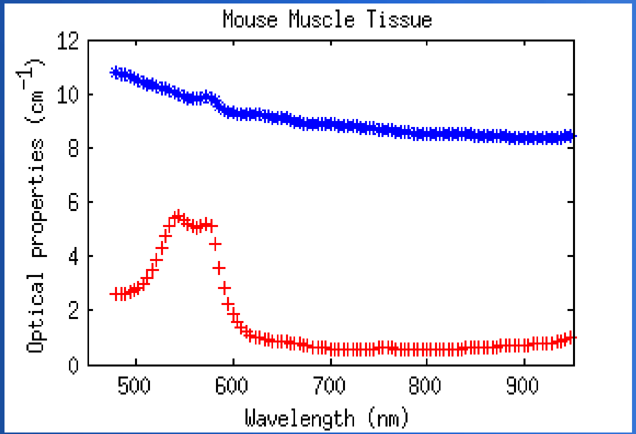
CR in medical physics



- Tissue has refractive index of about n = 1.4 → beta particles with T >220 keV emit CR
- Beta decay spectra of some radionuclides of biomedical interest
- Tissue optics described with absorption and scattering coefficients

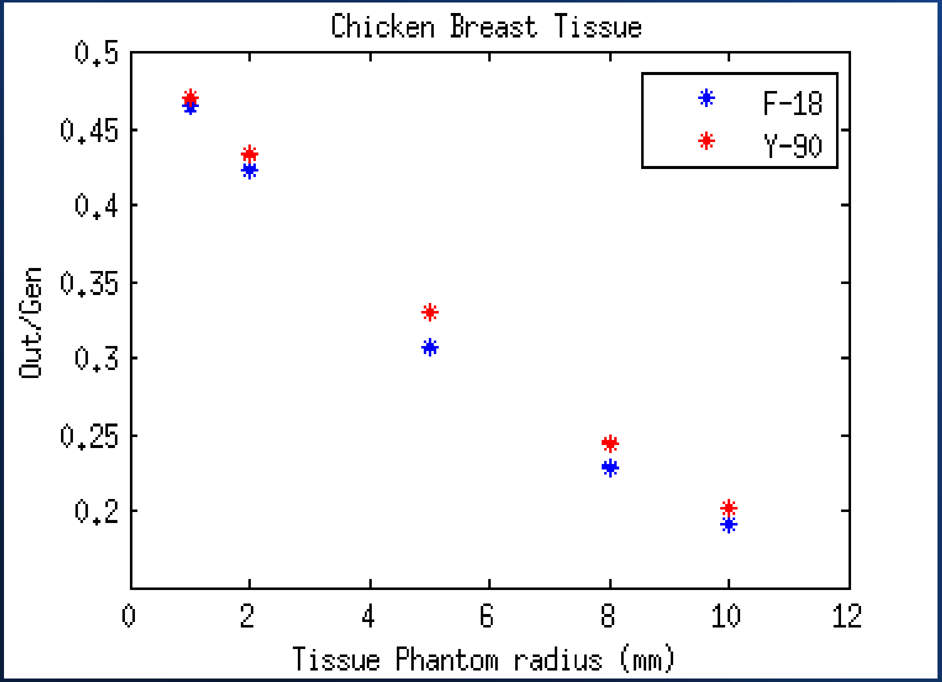
- UV and IR readily absorbed
- Visible short λ penetrates up to 2.5 mm
- Light with λ = 600-1600 nm can penetrate up to 10 mm in tissue

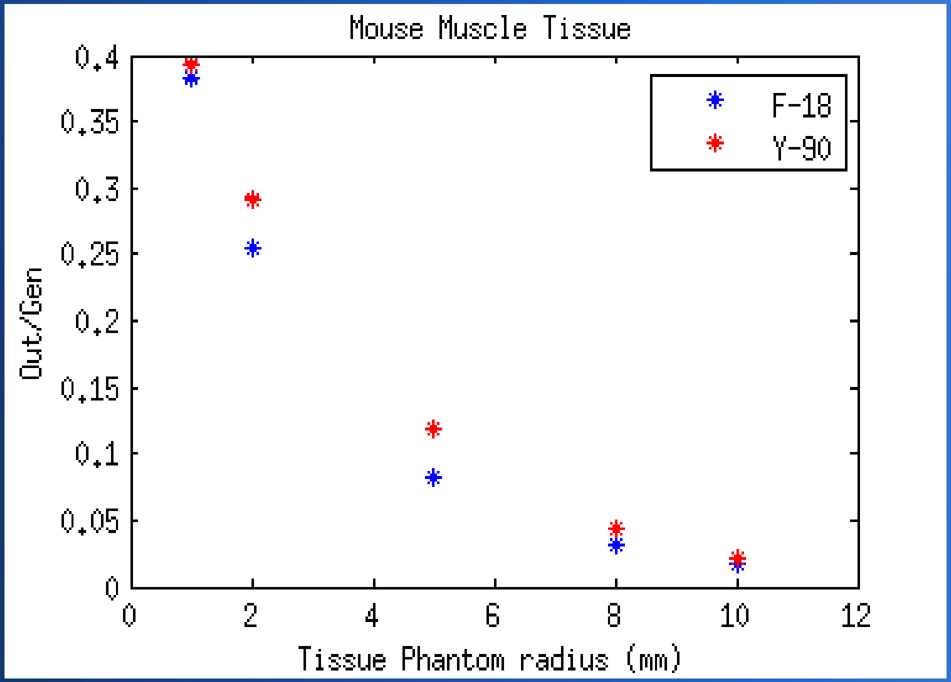




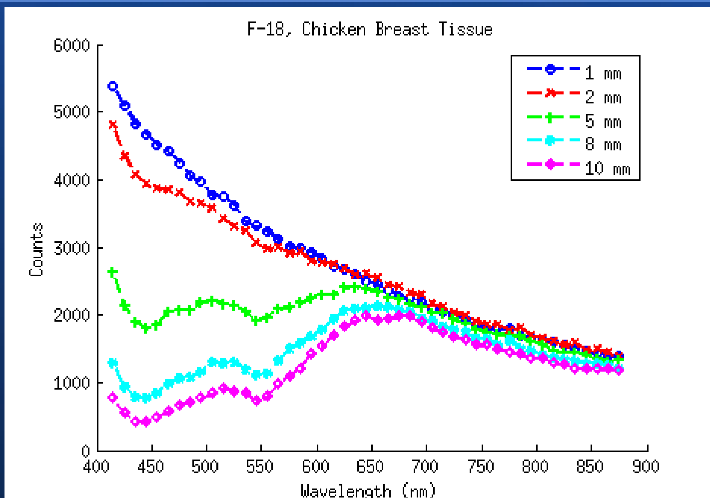
Tissue Attenuation

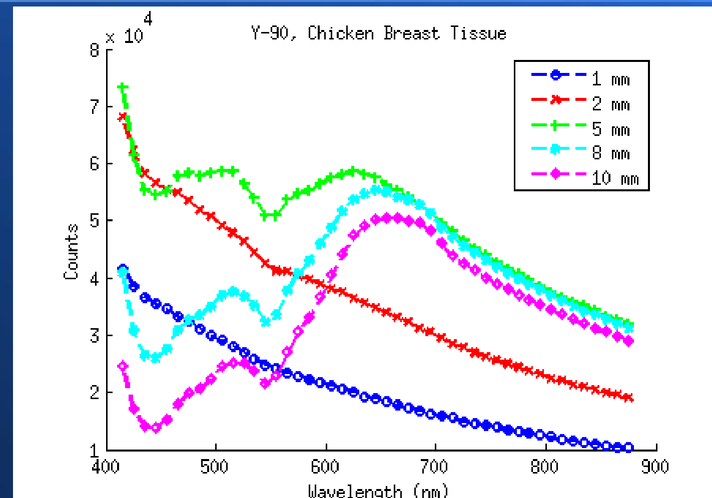
- Monte Carlo simulations of **tissue attenuation** → percentage of produced CR that escapes tissue as a function of the source depth in tissue
- Differences between radionuclides (light yield and Cherenkov emission range) and types of tissue

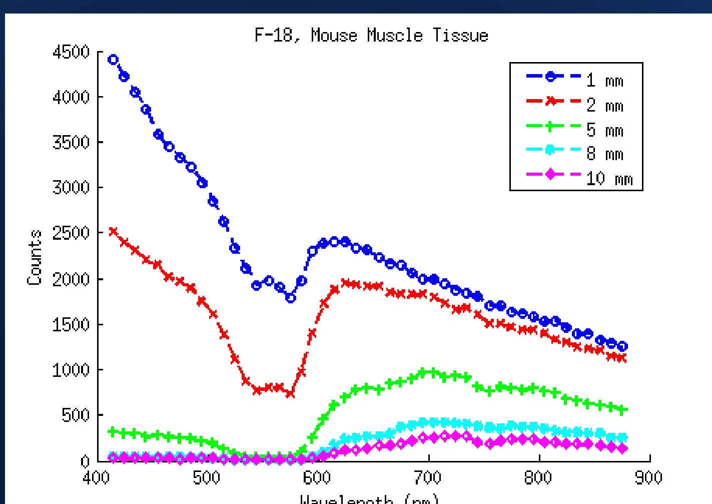


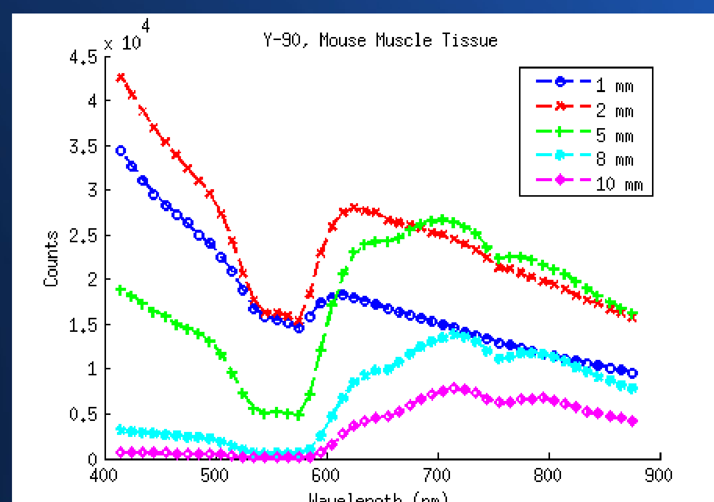


Transmission Spectra









- *Two radionuclides* → different light yield (y-axis)

2.4 vs. 69 photons per decay

[Mitchell 2011]

- *Different media* → different shape but same window of transparency

λ > 550 nm

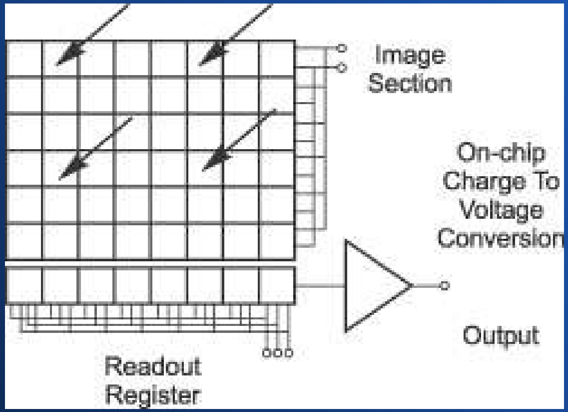
(green-yellow)

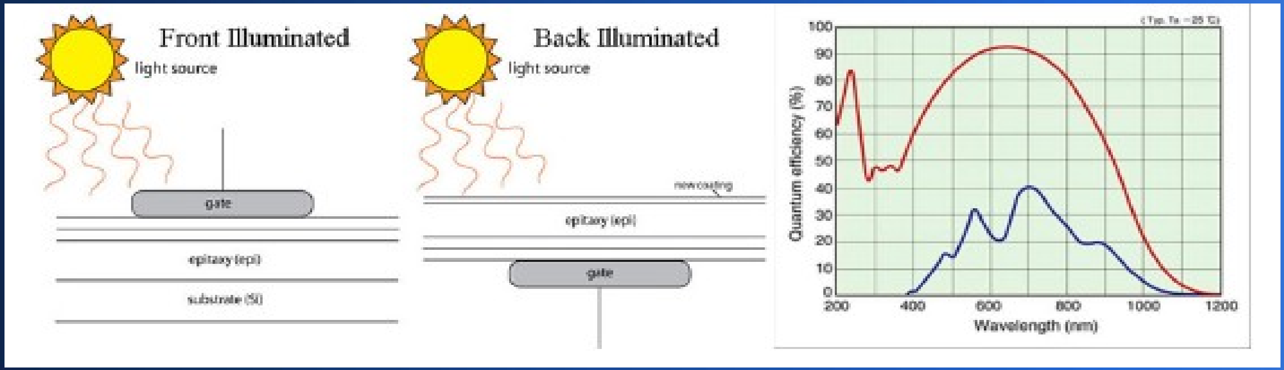
Scientific CCDs - requirements

Pixelated detector in which each pixel absorbs visible light and converts it to a proportional electrical signal that is read out via a shift register and a preamplier

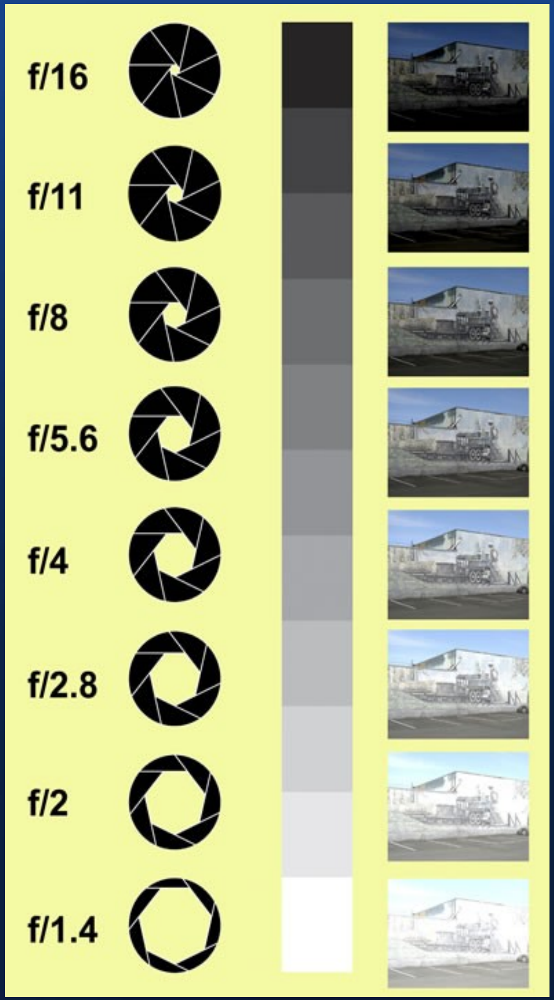
- CCD, EMCCD, ICCD, CMOS
- Low noise
- Strong cooling (reduced dark current → allows longer acquisition time)
- High QE

(back-illumination is preferred)





Lenses - requirements



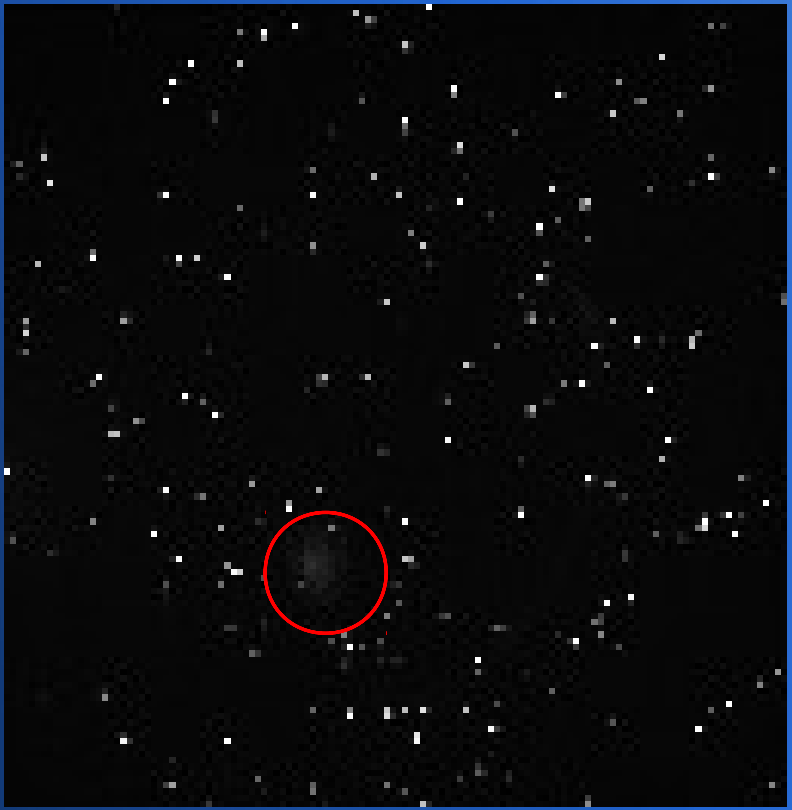
- Focal length: distance in air over which initially parallel rays are brought to a focus → about *25mm* is the most common and general
- F/number: ratio of the lens's focal length to the diameter of the entrance pupil, determines relative image brigthness → *as small as possible* (f/0.7 is current limit)
- Image circle: cross section of the cone of light transmitted by the lens → *diameter must be greater than the sensor size* to avoid vignetting (reduction of the image brightness at the corners)

- Transmission curve
- Window of transparency
- Mimimum working distance → *as small as possible* to reduce geometric divergence

Importance of f-number

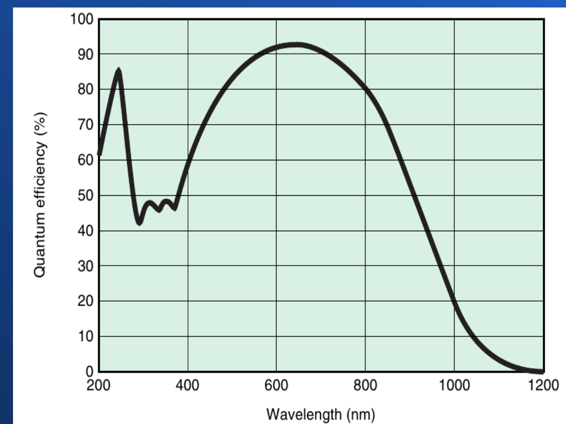
Acquisitions of 300 s images of 50 µCi pill of I-131 (Schneider f/1.8 lens)

f/1.8



f/4

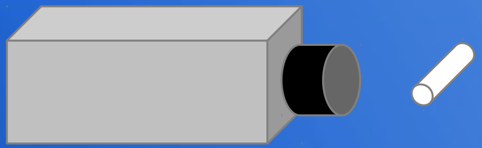
Final Setup



- ORCAII-BT-512G: high resolution, back-thinned and back-illuminated, air Peltier cooling to -65°C, 512x512 pixels, 24 µm size
- Schneider Xenon 25mm f/0.95: C-mount, MWD 200 mm, 16 mm image circle
- Dark box: PVC box with optical traps at openings, allows to vary source-to-detector distance

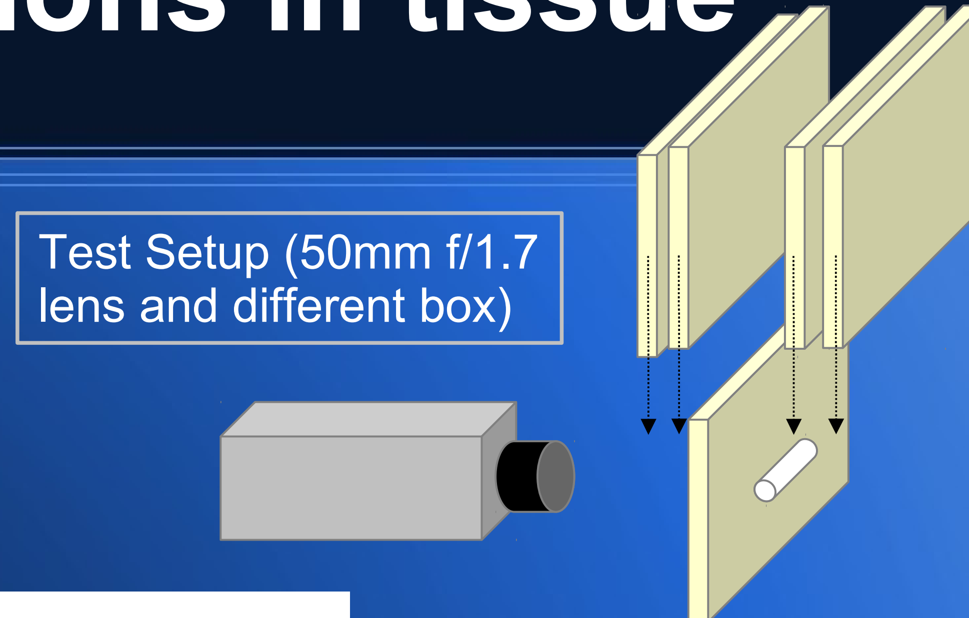
First acquisitions

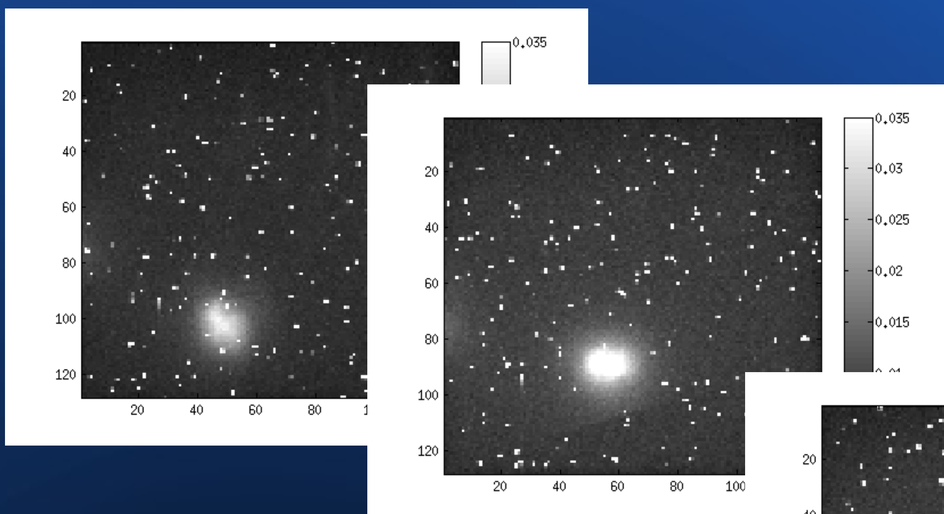
Test Setup (50mm f/1.7 lens and different box)

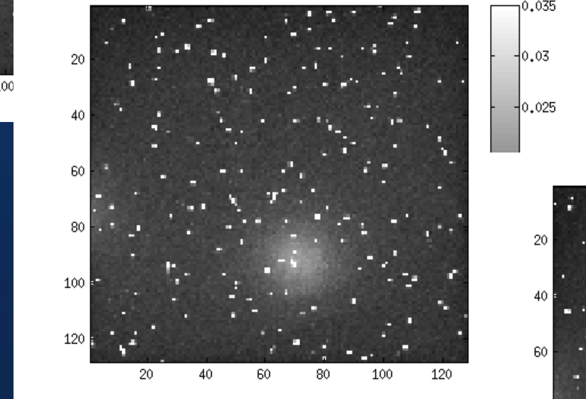


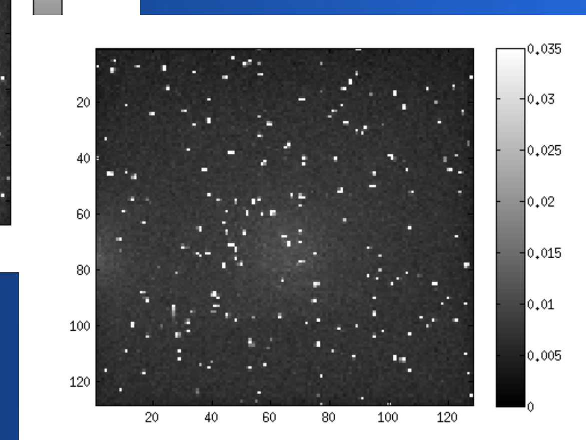
- 50 µCi pill of I-131 (β^-)
- T = 300 s
- Binning 4 (128x128 pixels)

First acquisitions in tissue





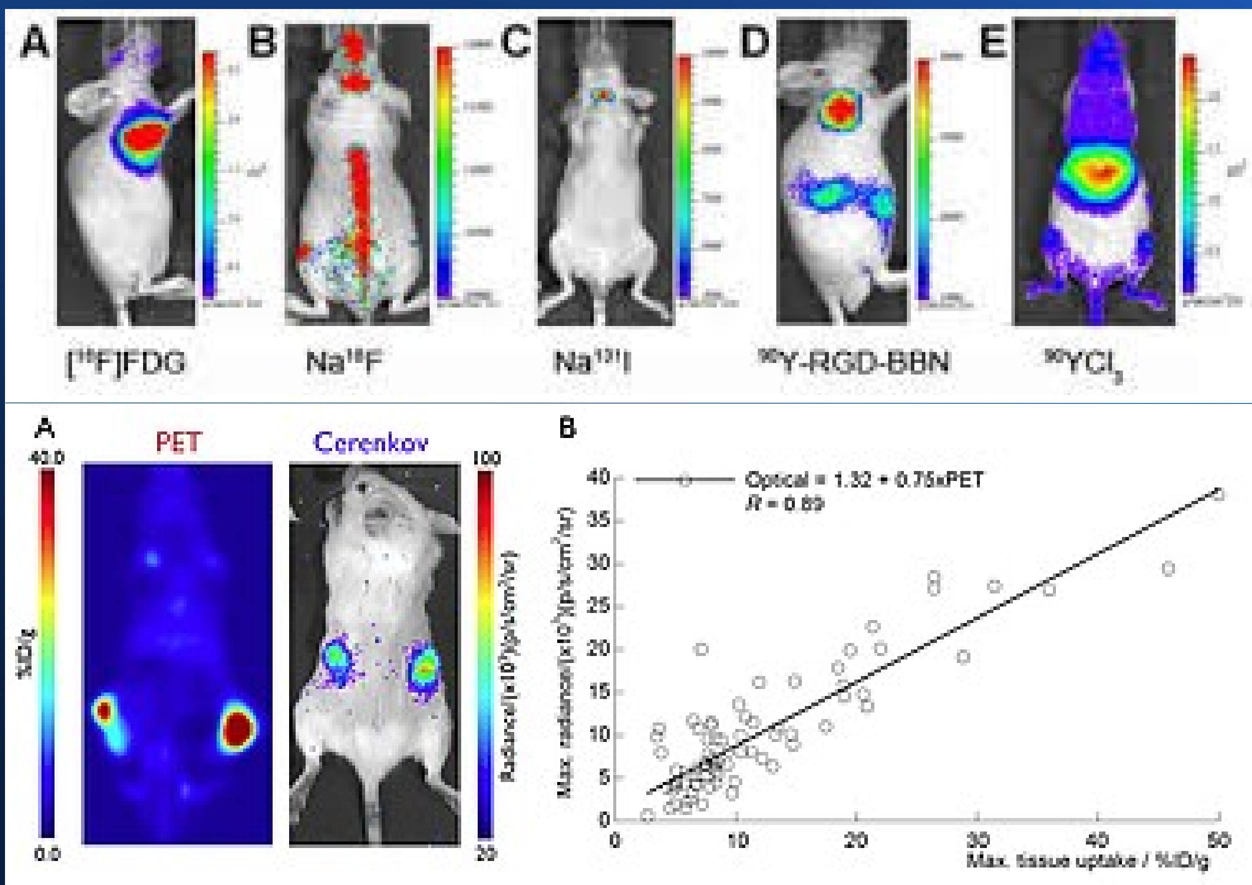




- 50 µCi pill of I-131 (β^-)
- Chicken breast slices
- 2-3 mm thickness each
- T = 300 s
- Binning 4 (128x128 pixels)

Potential Applications

Preclinical CLI



- direct measurement of the behaviour in tissue of β^- emitters

  http://www.biospacelab.com/

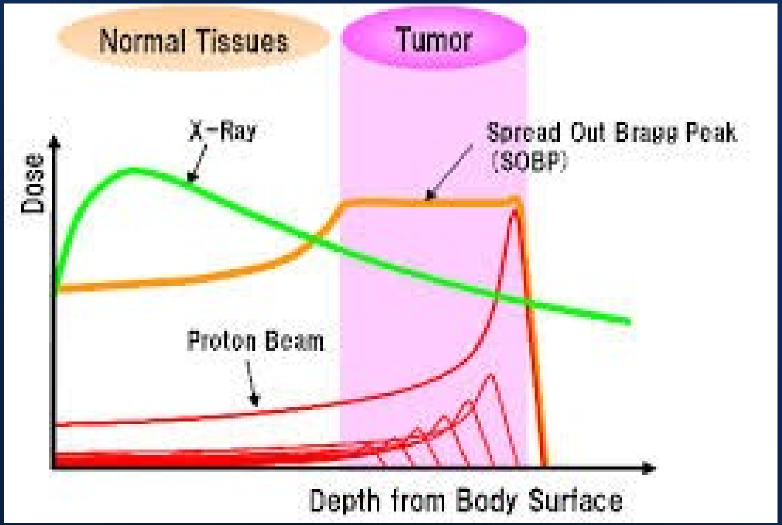
- quantitative comparison of the results with those of Positron Emission Tomography for β^+ emitters.

  http://www.mskcc.org/research/lab/jan-grimm/cerenkov-imaging

Potential Applications

Proton Therapy

- External beam radiotherapy that uses a beam of protons to irradiate a diseased tissue
- Precise dose delivery and normal tissue damage reduction
- Very expensive

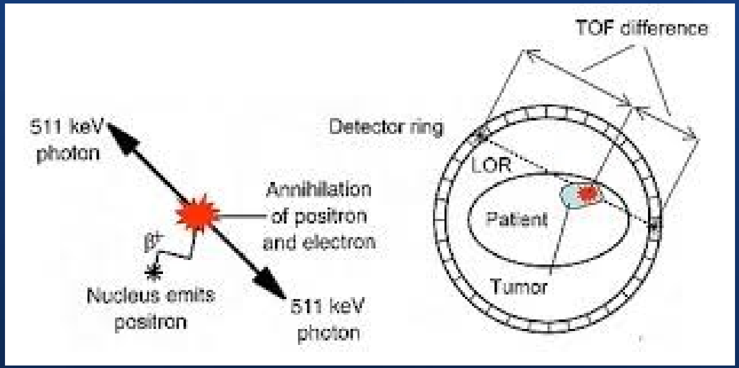


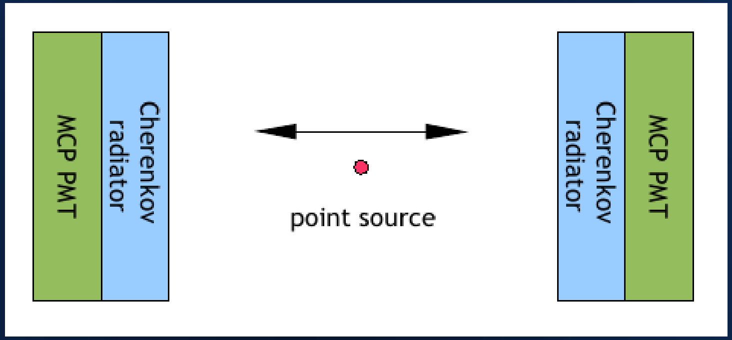
- **Prostate cancer** → Fiber-optic based rectal Cherenkov Luminescence probe to monitor the treatment and the tumour evolution

- **Optimization of proton therapy dose delivery in mouse** → preclinical studies are needed for an accurate treatment plan, CT maps provide anatomy, and radiator reduced dimension allows tomographic acquisition

Potential Applications

Others: Cherenkov TOF PET





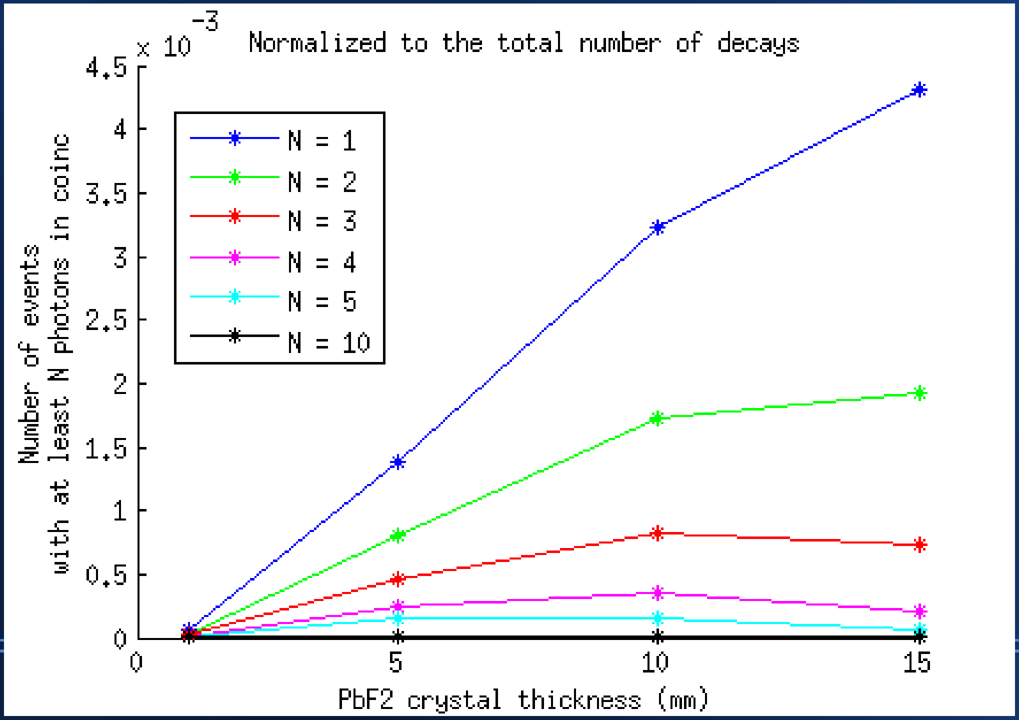
- **PET:** detection of tumour position and biochemical processes in the human body through the detection of the 511 keV annihilation photons of the β^+ emitted in the radioactive decay of a nuclide in tissue
- **TOF PET:** measures the difference between the times of arrival of the two annihilation photons at the detectors to improve spatial resolution
- **Cherenkov TOF PET:** detects prompt CR in appropriate radiators instead of the delayed scintillation radiation produced by the gammas in scintillators optically coupled to photodetectors [Korpar 2011]

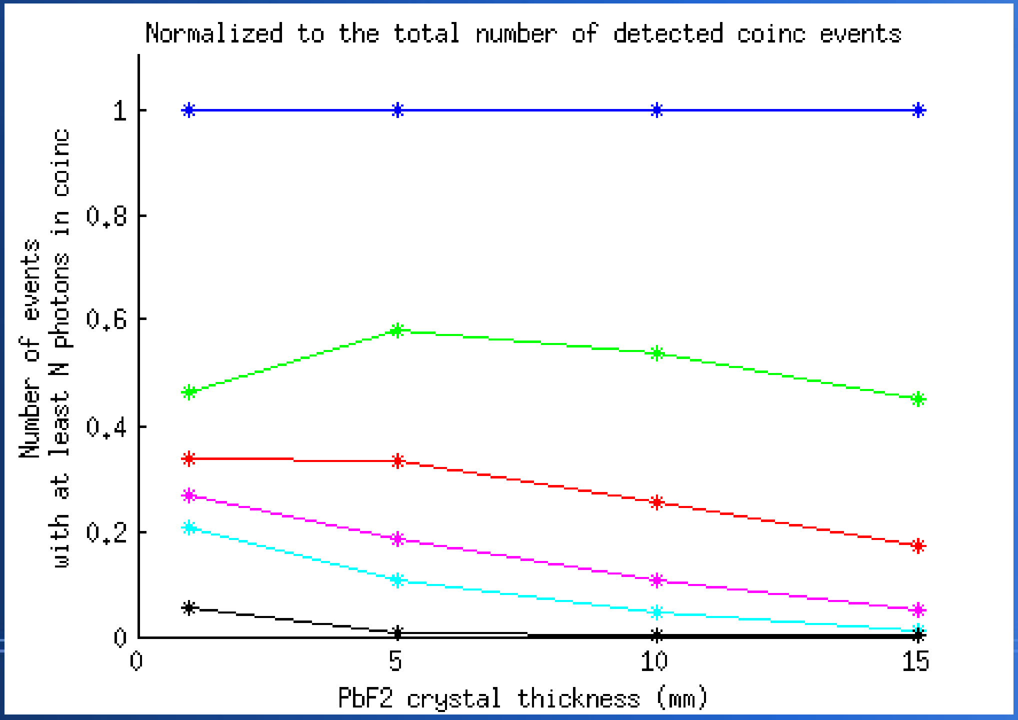
Potential Applications

Others: **Cherenkov TOF PET – Monte Carlo simulation**

Absolute detection efficiency of simulated setup (how many detectable events can be obtained out of a certain number of decays)

Relative detection efficiency of simulated setup (detection efficiency reduction as a function of the number of photons needed to detect the event)





Collaborations

Istituto San Raffaele di Milano, Dott. Spinelli

- development of a hybrid Monte Carlo code for a full description of a small animal CLI experiment
- poster ***Development of a simulation environment for Cherenkov luminescence imaging***, M Pagliazzi, E Ciarrocchi et al, at 2013 IEEE NSS/MIC/RTSD in Seoul, Korea, 27 October-2 November 2013

Imaging Research Lab, UW, Seattle WA, Prof. Miyaoka

- feasibility study of a new acquisition technique with Silicon PhotoMultipliers for Positron Emission Tomography
- talk ***A Depth of Interaction PET Detector Using Side Surface Readout***, RS Miyaoka, A Lehnert, WCJ Hunter, E Ciarrocchi, MG Bisogni, M Morrocchi, A Del Guerra at 2013 IEEE NSS/MIC/RTSD in Seoul, Korea, 27 October-2 November 2013

Conclusions

- Detection system requirements have been understood
- Detection system has been setup
- First qualitative CLI images have been obtained
- A potential application has been found
- Collaborations on different fields have been established to extend capacities and skills

Future Work

1. Optimization of proton therapy dose delivery in mouse (Exchange Program at UW)

- Monte Carlo simulation of the spatial and angular distributions of CR escaping from animal → does it allow to localize tumour? Is *imaging* possible or only *dosimetry*?
- Comparison (Monte Carlo + Experiments) to determine the best detection system: CCD vs. SiPMs with Single Photon Counting Capabilities? Focusing lens vs. compact optical fibers?

2. Optical system: data taking and description in Monte Carlo code (CCD + lens)

- Feasibility study on the system built
- Optimization of the acquisition procedure
- Complete code validation

This part will depend also on results obtained at point 1.

3. Cherenkov TOF PET → Evaluation of the absolute efficiency of the technique without modeling the geometric efficiency of the specific set-up

Thank you for your attention!

Protons and Alfas

Protons in Tissue do not emit CR

$$T = mc^2(\gamma - 1) \quad \Rightarrow \quad \beta = \sqrt{\frac{T^2 + 2Tm}{T^2 + 2Tm + m^2}}$$

$$T \simeq 200 \text{ MeV}, \; m_p \simeq 1000 \text{ MeV} \quad \Rightarrow \quad \beta \simeq 0.56 < 0.7 \quad (\text{soglia con n} = 1.4)$$

Alpha particle do not transfer enouh energy in a scattering event

$$Q = \frac{4m_0 m_\alpha}{(m_0 + m_\alpha)^2} = 5.5 \cdot 10^{-4}$$

$$E_\alpha \simeq 5.5 \text{ MeV} \quad \Rightarrow E_{el} \simeq 2.8 \text{ keV}$$